TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM

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Dedicated

to

my family

&

teachers

Acknowledgement

"Dissertation writing is the stepping stone to research dynamism"

It is not just a mere formality to write an acknowledgement but it is my duty to pay the due respect, a sense of gratitude from the core of my heart to all those who have encouraged, inspired and guided me at each and every step of my work.

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Dr Harmanjot Kaur Walia

LIST OF ABBREVIATIONS

AD- Autosomal Dominant

AVC- Aortic Valve Calcification

BMD- Bone Mineral Density

CAD- Coronary artery Disease

CaSR-Calcium sensing receptor

CVA- Cerebrovascular Accident

DEXA- Dual-energy x-ray absorptiometry

DM- Diabetes Mellitus

ECG- Electrocardiography

ECHO- Echocardiography

EF-Ejection Fraction

FHH- Familial hypocalcemic hypercalcemia

FIHP- familial isolated hyperparathyroidism

FS- Fractional Shortening

GAD-7- Generalised Anxiety Disorder-7

hPTH - human Parathormone

hPTHrp - human Parathormone related peptide

HPT-Hyperparathyroidism

HPT-JT- Hyperparathyroidism with jaw tumour

HRPT2- Hyperparathyroidism-2 with jaw tumours

HTN - Hypertension

ITA- Inferior Thyroid Artery

IVSD- Inter Ventricular Septal Diameter

LVH-Left Ventricular Hypertrophy

LVID- Left Ventricular Internal Diameter

LVM- Left Ventricular Mass

LVMI-Left Ventricular Mass Index

LVPW- Left Ventricular Posterior Wall

MDD- Major Depressive Disorder

MEN-1-Multiple Endocrinal Neoplasia-1

MEN-2A- Multiple Endocrinal Neoplasia-2A

NS-HPT- Neonatal Severe Hyperparathyroidism

PAH- Pulmonary Arterial Hypertension

PH- Pulmonary Hypertension

PHPT-Primary Hyperparathyroidism

PHQ-9- Patient Health Questionnaire-9

PTH- Parathormone

PTHrp- Parathormone related peptide

PUD- Peptic Ulcer Disease

RET- Rearranged during Transfection

RLN- Recurrent Laryngeal Nerve

SPECT- Single-photon emission computed tomography

TSG- Tumour Suppressor Genes

VPC- Ventricular Premature Contraction

ABSTRACT

Introduction: Primary hyperparathyroidism is a disease characterised by inappropriate or unregulated overproduction of parathormone associated with hypercalcemia. Calcium being very important element in various physiological processes, the disease is associated with multisystem presentation- mainly bony, renal, gastrointestinal and neuropsychiatric.

Aim of the Study: The proposed research aims to evaluate clinical profile of patients presenting with primary hyperparathyroidism in tertiary care hospital.

Materials & methods: This prospective cross-sectional observational study was conducted at DMCH Ludhiana from 15th September 2022 to 31st December 2023. The study group included 128 patients admitted in the hospital or presenting to OPD. The patients were assessed for clinical presentation and outcome in accordance with treatment provided.

Results: PHPT is primarily the disease of elderly female with M:F 1:1.7. The presenting symptoms according to prevalence were bony (44.1%), gastrointestinal (43.4%), neuropsychiatric (40.6%), renal (31.3%) and asymptomatic (16.4%). Biochemically the disease was associated with high serum calcium, high PTH, low hemoglobin, high NLR, low platelet counts, high ALP, hypovitaminosis-D and hypophosphatemia. The patients also had increased cardiac morbidity. The lesion was most commonly localized to inferior gland. Treatment usually consisted IVF with diuresis, calcitonin, cinacalcet and in the non-responders zoledronate, denosumab or hemodialysis was done. On follow-up patients had decreased mean calcium and PTH levels. The disease was associated with 2.3% mortality.

Conclusion: PHPT is third most common endocrinal disorder after diabetes and thyroid disorders yet is mostly underdiagnosed and undertreated. Routine serum calcium analysis and high index of suspicion by physician can help decreasing patient morbidity significantly by offering them curative surgical intervention.

Keywords: Denosumab, Primary hyperparathyroidism, PHPT, Renal calculi, Serum calcium, PTH, Pancreatitis, Zoledronate,

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INTRODUCTION

The parathyroid glands were the last organ to be discovered in the human body, located parallel to thyroid hence justifying the nomenclature- parathyroid glands. Mostly humans have four glands, two superior and two inferior with development starting at fifth week of intrauterine development.[1,2] Superior parathyroid develops from fourth branchial pouch and are present on posteromedial aspect of thyroid gland near tracheoesophageal groove. Inferior parathyroid glands develop from third branchial pouch which are located on posterior to thyroid in superior mediastinum along the path of descent of thymus. Both the glands are chiefly supplied by branches of ITA.[3]

An inappropriately high PTH for particular corrected serum calcium level is considered hyperparathyroidism. It is of three types- primary, secondary, tertiary.

Table 1- Tabular representation of types of hyperparathyroidism.[1]

HYPERPARATHYROIDISM			
	PRIMARY	SECONDARY	TERTIARY
PTH	↑↑	↑	↑↑↑
Calcium	↑	↓/N	↑
Phosphate	↓	↑/N	↑
Vitamin D	↓/N	↓↓↓	↓/N
Etiology	-Parathyroid adenoma, hyperplasia, carcinoma -Chronic Lithium therapy -MEN1 -MEN2A	- Failure of Chronic renal - Deficiency of Vitamin D	- Chronic renal failure

PHPT is the most common type of HPT which is a biochemical syndrome characterised by inappropriately high PTH due to increased PTH secretion from the parathyroid glands.[1,4] It is most frequently attributed to parathyroid adenoma (85-90%) followed by hyperplasia(5-10%) or parathyroid carcinoma (1 %).[4]

In general medical practice, this disorder is marked by hypercalcemia, an increased or inappropriately normal PTH level, and often a low serum phosphate level resulting from renal phosphate wasting. Risk factors for PHPT include neck irradiation, lithium therapy, genetics.[5] The genes implicated in sporadic pathogenesis are calcium-sensing receptor (CaSR)(under expression leads to continued secretion of PTH from gland), vitamin-d receptor and cyclin D1 (overexpressed).[1] A newer phenotype of PHPT is characterized by elevated serum PTH levels while serum calcium levels remain normal. This condition is often diagnosed during evaluations for nephrolithiasis or metabolic bone disease.[5] The related syndromic disease group constitute MEN 1-5 and HPT-JT. The non-syndromic group comprises FHH 1-3, NS-HPT and FIHP.[6] FHH is associated with loss of function mutations in the calcium-sensing receptor (CaSR) usually have mild hypercalcemia and often result in a benign clinical course.

Clinical presentation of PHPT is clinically characterised by a pentad including bones, stones, abdominal pains, psychic moans and fatigue overtones. In western world PHPT is usually detected in asymptomatic phase due to routine biochemical serum calcium screening, whereas in developing nations still patients are diagnosed in symptomatic phase. Skeletal manifestations range from bony pains to recurrent fractures with rarely findings of OFC (osteitis fibrosa cystica) and brown tumours. Osteoporosis affects 50-65% of patients with PHPT. Osteitis fibrosa cystica with brown tumour formation is a classic yet uncommon manifestation of PHPT, seen in 2-5% of patients.[7]

Renal manifestations include nephrocalcinosis with frequency varying from 15-20 %. Delayed diagnosis can present with multiple recurrent renal colic, hydroureteronephrosis with deranged renal functions. Compromise in renal concentrating ability can result in polyuria and polydipsia. According to Banerjee *et al.* presence of nephrolithiasis, elevated serum calcium multiplied by phosphate (Ca x P) levels and PTH levels were positively associated with concomitant renal dysfunction.[8]

Gastrointestinal manifestations of PHPT are nausea, constipation, pain abdomen, pancreatitis and gall stone disease. In west pancreatitis is not considered as complication of PHPT due to very mild and short duration of hypercalcemia, however in developing countries pancreatitis is reported in 10-20 % patients. According to Arora *et al.* [9] acute pancreatitis as initial manifestation is quite rare. Study also concluded presence of nephrolithiasis was significantly associated with acute pancreatitis, and patient with PHPT induced pancreatitis had higher serum calcium levels with lower frequency of renal manifestations than PHPT without pancreatitis. In patients with MEN1, duodenal ulcers may arise from pancreatic tumors associated with excessive gastrin secretion.[10]

Cardiovascular conditions such as cardiac functional abnormalities, left ventricular hypertrophy, and endothelial dysfunction have been documented.[10] Neuropsychiatric symptoms encompass a broad spectrum, including anxiety, depression, irritability, changes in mental status, cognitive impairment, sleep disturbances, dementia, reduced quality of life, delirium, psychosis, and hallucinations.[7] Hematological manifestations are quite common in symptomatic PHPT with anaemia is most common with prevalence of 30-40%.[1]

Biochemical changes aiding diagnosis include persistently elevated PTH levels in the presence of hypercalcemia and hypophosphatemia. Other investigations include evaluation for creatinine clearance, elevated 24-h urinary calcium. Nephrolithiasis or nephrocalcinosis can be identified

using X-ray, ultrasound (USG), or CT scans. The BMD measurement by DEXA is recommended for skeletal survey, assessing T scores <-2.5 at the lumbar spine, total hip, femoral neck, or distal 1/3 radius.[10] Genetic assessment should be recommended for those patients who are under 30 years old, those with multiglandular disease indicated by history or imaging, and/or individuals with a family history of hypercalcemia or syndromic diseases.[11] Ultrasonography is often used as first modality to localise abnormal parathyroid gland, it is cost effective and also has a reasonably good sensitivity and specificity. 99m-Tc scintigraphy is often complementary to ultrasonography while it has better sensitivity and specificity than USG. In case of failure of localisation or discordant analysis choline and methionine positron emission tomography with nearly 100 % sensitivity and specificity can be used in selected patients.[1,12]

Abnormal gland excision acts as the mainstay of the treatment. However, for patients with mild or asymptomatic disease, especially elderly individuals, medical surveillance without intervention is often recommended. Evidence favouring surgery is growing due to skeletal, cardiovascular, neuropsychiatric manifestations and their reversibility post-surgery. After successful surgery, a decrease in serum calcium typically occurs within 24 hours, and calcium levels in blood usually drop which can rarely induce HBS.[10]

In the medical management of hypercalcemic crisis, initial treatment involves hydration with increased salt intake and forced diuresis. The primary goal is to restore normal hydration and normalize serum calcium levels, which typically begin to decrease within hours. Antiresorptive therapies such as intravenous bisphosphonates, subcutaneous denosumab and calcimimetic agents such as cinacalcet constitute medical therapy. I/V infusion of zoledronate 5 mg over half an hour reduces serum calcium over 24-48 hours.[1,13]

Asymptomatic patients should undergo regular monitoring, including biannual checks of serum calcium, annual assessments of serum creatinine, and annual bone density scans (covering the lumbar spine, hip, and forearm). Parathyroidectomy may be recommended even in asymptomatic based on clinical indications.[14]

Symptomatic PHPT is associated with increased mortality and morbidity. Common causes of mortality include renal failure, respiratory exhaustion secondary to flail chest, pancreatitis and sepsis. Morbidity with persistent abnormalities after curative parathyroidectomy are bony deformities, low bone mineral density, renal dysfunction and secondary diabetes-secondary to pancreatitis.[1]

AIMS & OBJECTIVES

The proposed research aims to evaluate clinical profile of patients presenting with primary hyperparathyroidism in tertiary care hospital.

REVIEW OF LITERATURE

The parathyroid glands were the final organ identified in the human body. Positioned alongside the thyroid glands, their name "parathyroid" reflects their parallel location. Each person typically has two superior and two inferior parathyroid glands, with each gland weighing around 25 mg on average.[10] Superior parathyroid glands are situated superior to ITA (Inferior Thyroid Artery) and posterolateral to RLN (Recurrent Laryngeal Nerve) bilaterally. Arterial supply is by branches of ITA with venous drainage via thyroid veins (superior, middle, inferior). Ectopic glands mostly visible along the path of embryological descent resulting from aberrant migration, within the carotid sheath, superior part of mediastinum, retroesophageal or intrathyroidal, with a meta-analysis revealing 16% ectopic parathyroid gland prevalence.[15,16] Supernumerary parathyroids have been found in 13 % of the autopsies.[16]

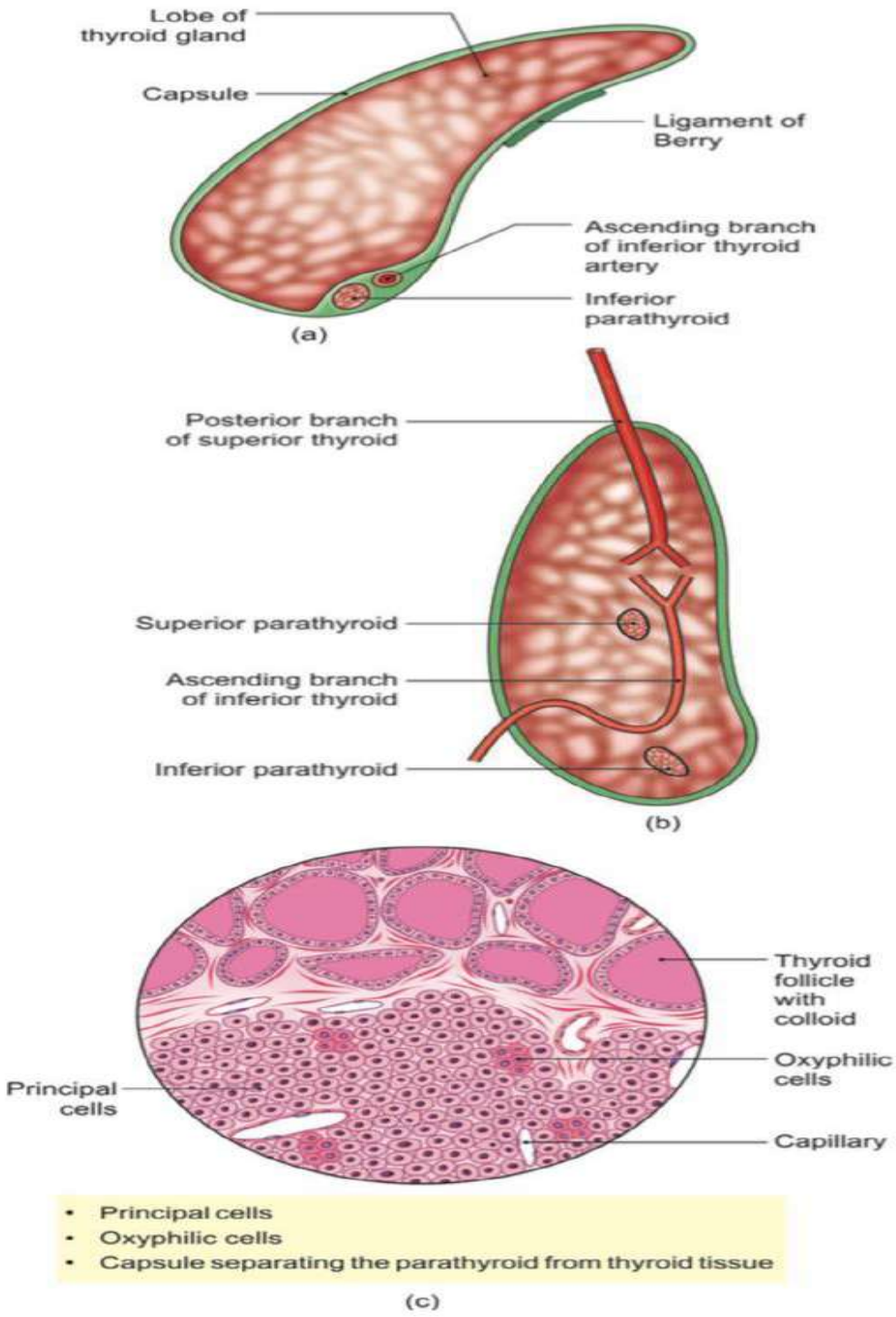


Figure 1- Parathyroid glands a) Transverse section b)Posterior view c)Histology [17]

Historical perspective:

Parathyroid gland was first observed in 1849 by Richard Owen, while dissecting an Indian rhinoceros and he described the small yellowish structures as “the size of small peas” attached to the thyroid gland.[18] However, In 1880, glandula parathyroideae was first histologically described by a Swedish anatomist Ivar V Sandstrom. A German pathologist, Friedrich Daniel Von Recklinghausen, in 1891 described the severe deterioration of the skeleton explained as OFC (osteitis fibrosa cystica), but the first association between bone and parathyroid gland was made by J Erdenheim. Initially, physicians believed that the enlargement of the glands was caused by the bone disease.[18] In 1925, Felix Mandl reported the first successful surgical intervention for PHPT.[19]

In 1935, Fuller Albright and colleagues noted that most patients with PHPT not only had bone disease but also renal calculi. For many years, this combination was regarded as the defining characteristic of PHPT.[20] Up until the early 1960s, surgery for PHPT was performed primarily to address its overt symptoms. However, in the mid-1960s, the number of operations surged as more patients began receiving treatment earlier in the disease's progression, often with fewer symptoms. A significant shift occurred in the early 1970s with the advent of automated serum calcium measurement. This development allowed for the frequent identification of patients through their biochemical profiles, transforming the presentation of PHPT from a condition characterized by severe neuromuscular, bony, and renal symptoms with pronounced hypercalcemia to a milder or even asymptomatic disease. [20]

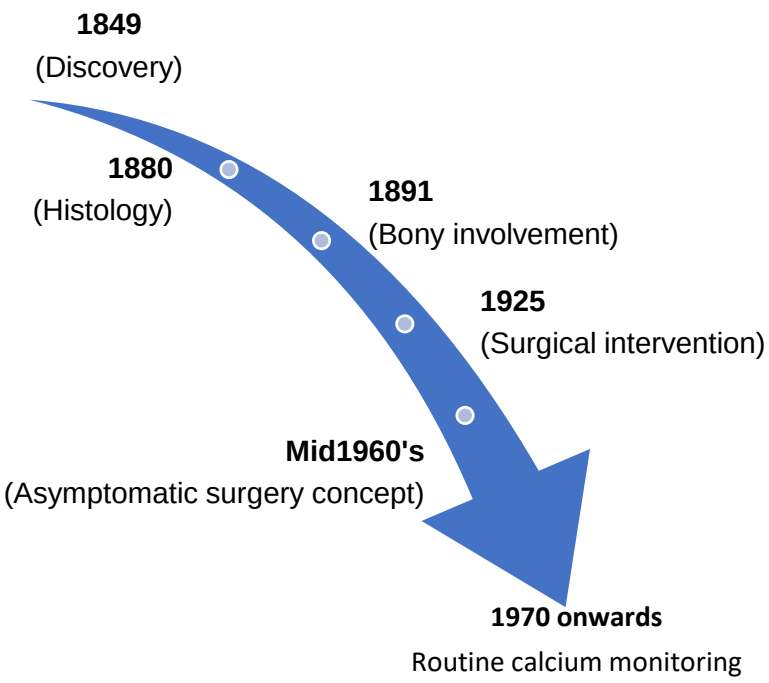


Figure 2- Advancement timeline of parathyroid gland [18, 19, 20] Refer to data in text for details

The surgical approach to parathyroidectomy has evolved from a comprehensive neck exploration to a minimally invasive intervention. The modern technique has fewer complications and is generally well-tolerated by most patients.[21,22] The surgical development was primarily possible due to pre-operative radiological diagnostics that enable accurate pre-surgery localisation.

Embryology & histology:

The glands develop from the IIIrd and IVth branchial pouches: the third pharyngeal pouch forms the inferior parathyroid glands, while the fourth pharyngeal pouch forms the superior parathyroid glands. Because the inferior glands descend a relatively long distance, their positioning is more likely to vary. Parathyroid glands are composed of two types of cells: chief (with clear cytoplasm) and oxyphil cells (with eiosinophilic granular cytoplasm)[1,15].

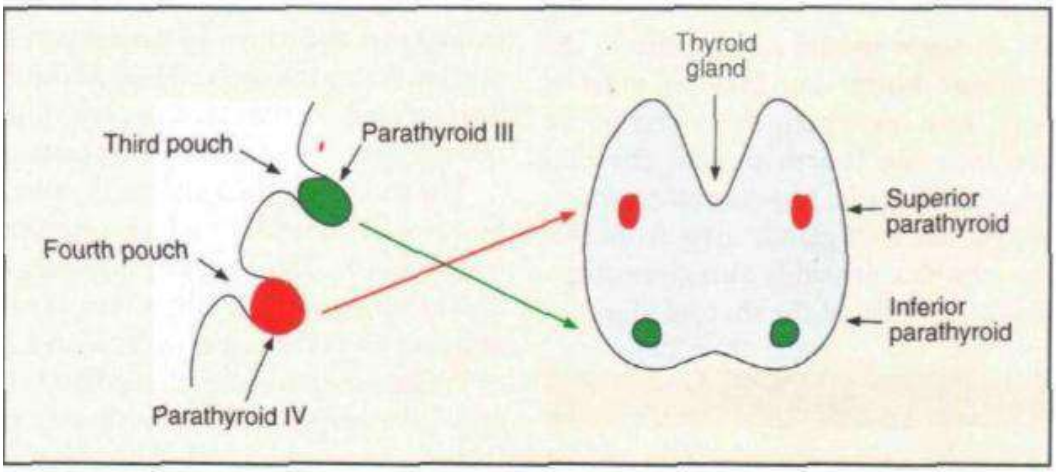


Figure 3- Derivation of superior and inferior parathyroid glands. (Relative position of parathyroid III and IV is reversed)[23]

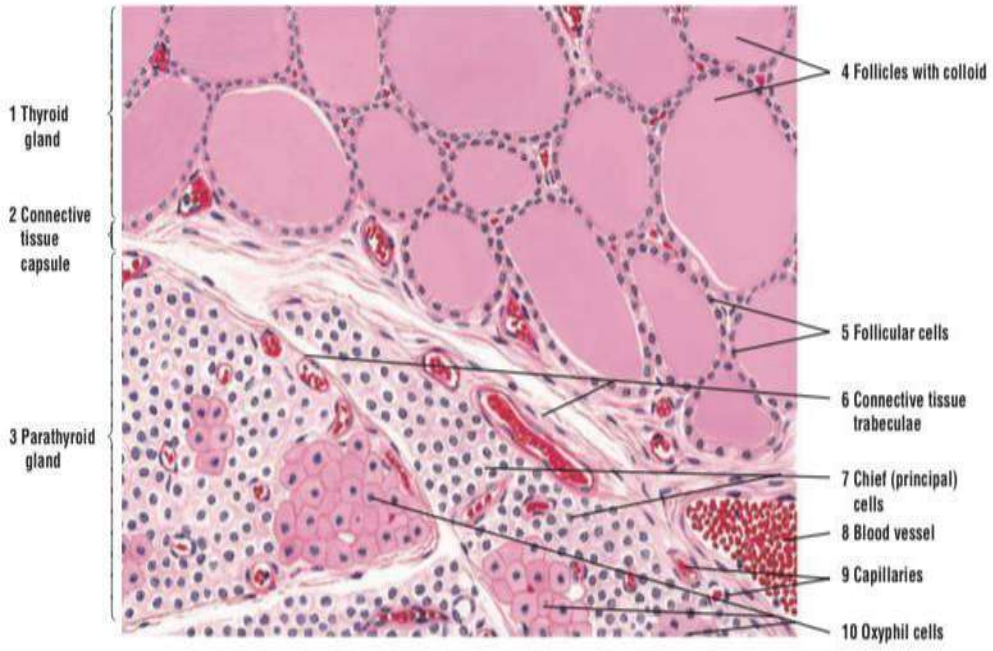


Figure 4- Histopathological representation of thyroid and parathyroid gland (canine view) Staining: H&E staining [24]

Physiology:

In adult humans, the parathyroid gland primarily consists of chief cells, with a small to moderate number of oxyphil cells, which may be absent in younger individuals. Chief cells are thought to be the main source of PTH secretion. The parathormone is a heat labile peptide consisting of 1-84 amino acids. PTH is only 84 amino acid long while PTHrp may be >139 amino acid long. 10 amino acids in PTH and PTHrp are identical while 20 out of 30 are homologous. The exact function of oxyphil cells remains unclear, but they are thought to be modified or depleted chief cells that no longer produce hormones.[25]

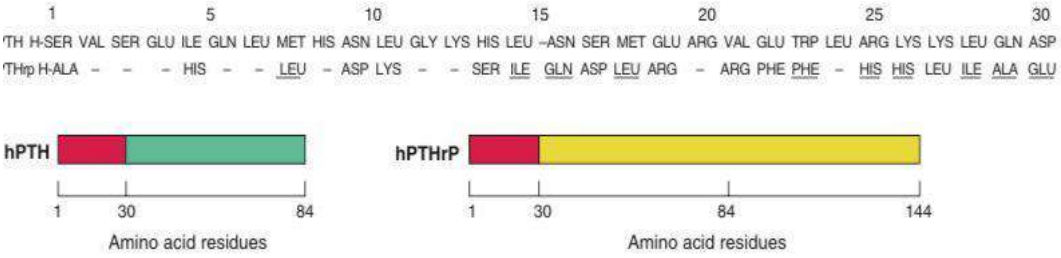

1 5 10 15 20 25 30
TH H-SER VAL SER GLU ILE GLN LEU MET HIS ASN LEU GLY LYS HIS LEU -ASN SER MET GLU ARG VAL GLU TRP LEU ARG LYS LYS LEU GLN ASP
THrp H-ALA - - - HIS - - LEU - ASP LYS - - SER ILE GLN ASP LEU ARG - ARG PHE PHE - HIS HIS LEU ILE ALA GLU
hPTH
1 30 84
Amino acid residues
hPTHrP
1 30 84 144
Amino acid residues

Figure 5- Schematic structure of similarities and differences amongst hPTH and hPTHrp [10]

PTH has circulating T½ of 3 to 4 minutes. It is metabolised by kidney and liver. Normal range of PTH is 10-65 pg/ml. PTH has ultradian secretion, peaking early morning with nadir in late afternoon with small peaks in late afternoon. Also, PTH secretion is closely linked to serum calcium, phosphate and active vitamin-D levels. Main function of PTH is to maintain serum calcium levels through peripheral organs; bone, kidney and intestines.[1]

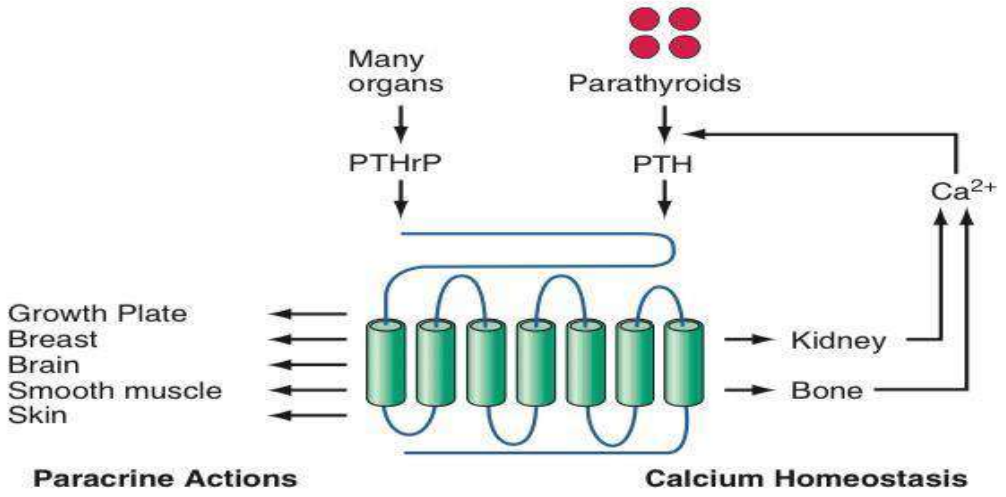


Figure 6- Dual role of the PTH/PTHrp receptor (PTHR1) [10]

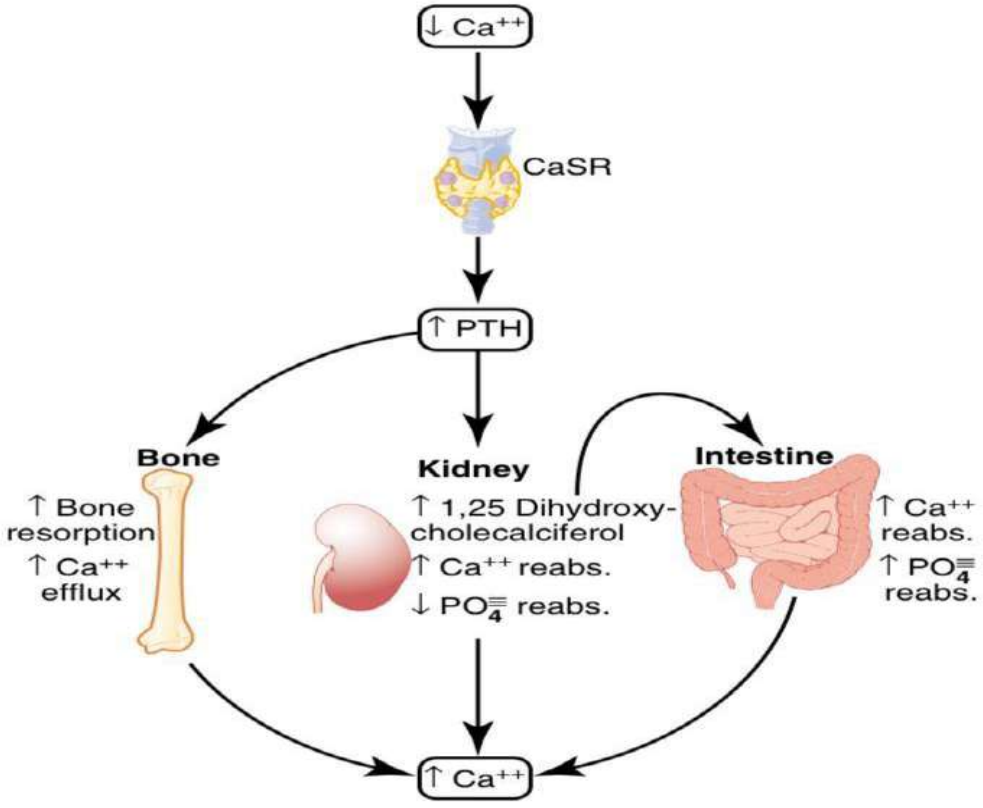


Figure 7- Effects of PTH on bone, kidney and intestines in response to altered serum calcium.[10]

Calcium homeostasis:

Maintaining a normal serum calcium concentration is essential for proper bodily function and plays a critical role in a variety of intricate cellular processes.[26] PTH and vitamin D regulate calcium homeostasis through a negative feedback mechanism to maintain calcium concentration within a narrow physiological range. Therefore, even minor changes in serum calcium levels can trigger significant secretory responses [27].

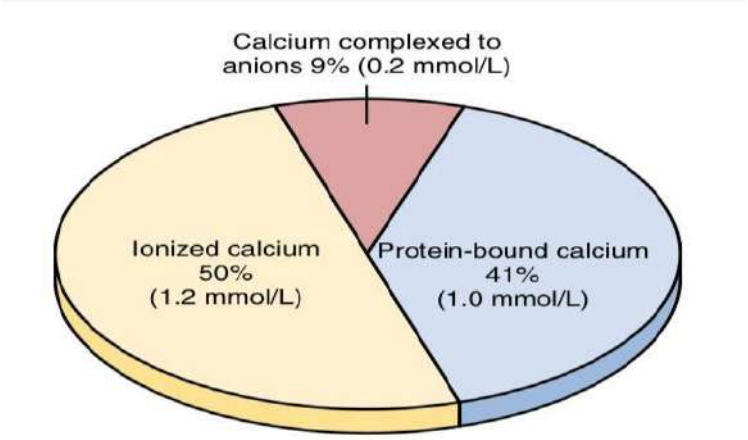


Figure 8- Distribution of ionised calcium, diffusible but unionised calcium complexed to anions and non-diffusible protein-bound calcium in plasma.[25]

In the adult body, approximately 1 to 1.5 kg of calcium is distributed, primarily bound as hydroxyapatite in the skeleton—a compound of calcium and phosphorus. Only about 1% of the total calcium is found in extracellular plasma, with roughly half bound to proteins, predominantly albumin, while the remainder is stored intracellularly. Calcium exerts its effects in its ionized form (Ca^{2+}) through:

- Influencing neuronal and muscle cell sensitivity by affecting intracellular signalling

- Serving as a co-factor in enzymatic reactions

- Acting as the most potent inhibitor of PTH secretion by binding to the calcium-sensing receptor (CaSR) on the membrane of parathyroid cells [28]

Even in diseased patients studies report remarkably normal level of calcium over decades which can be attributed to the concept described by Parfitt *et al.* in 1979 as equilibrium hypercalcemia due to a set point error. [29,30] Equilibrium hypercalcemia is characterised as serum calcium level above normal reference value which is maintained at the same level associated with few fluctuations over years. The hypothesis was that in mild to moderate PHPT this pattern seen due to increased bone resorption leading to hypercalcemia being balanced by an increased renal tubular calcium excretion. [31]

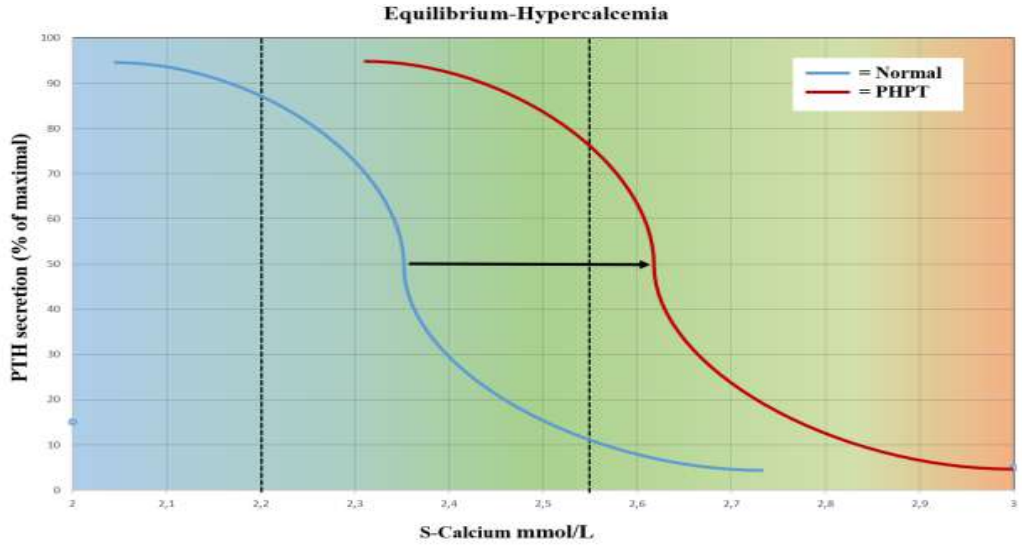


Figure 9- Model of equilibrium hypercalcemia (blue= normal physiology and red=PHPT). Dotted lines = upper and lower reference values for serum calcium (mmol/l). [30]

Hyperparathyroidism:

Abnormally excess secretion of parathormone is termed as hyperparathyroidism, which can be classified as primary, secondary or tertiary hyperparathyroidism.[32]After diabetes and thyroid disease, primary hyperparathyroidism is third most common endocrinal disorder affecting upto 0.1% of general population.[33] PHPT is more frequently seen in the women with ratio (F:M; 2-3:1) in developing countries whereas (F:M; 4:1) in western population. PHPT is considered as the disease of postmenopausal women all over world however any of the age groups can be affected with PHPT. [32]

Primary hyperparathyroidism refers to inappropriate or unregulated overproduction of parathormone resulting in increased renal absorption of calcium, leading to phosphaturia leading to hypophosphatemia, increased synthesis of 1,25-dihydroxy vitamin-D (which increases intestinal calcium absorption) and increased bony resorption ultimately resulting in hypercalcemia.[34]

There are three different pathological lesions inducing PHPT: [35]

- ✓ Adenoma – Adenoma is the benign most common parathyroid neoplasm in upto 85% of the cases of PHPT usually affecting only a single gland
- ✓ Hyperplasia – Hyperplasia refers to an expansion of hormonally active cells affecting all glands (multiglandular), occurring without a discernible stimulus for excessive PTH secretion. This condition accounts for about 10% of all cases of PHPT and can be linked to genetic abnormalities seen in inherited multiple endocrine neoplasia.
- ✓ Carcinoma – Carcinoma is an uncommon occurrence, accounting for less than 1%

The disease is most commonly attributed to a solitary parathyroid adenoma, which arises sporadically. Parathyroid hyperplasia (diffuse or nodular) accounts for 5-10% of cases, while carcinoma is extremely rare, representing about 1% of cases of PHPT.[1]Adenomas are mostly located in inferior gland however in 6-10 % ectopic tissue in thymus, thyroid, pericardium or retroesophageal can be located. Adenoma weight usually ranges between 0.5-5 g. Chief cells are prevalent in both adenomas and hyperplasia, characterized by a histologically the chief cells arranged uniformly. The disappearance of fat in the histopathology sample indicates the hyperplastic changes.[32]

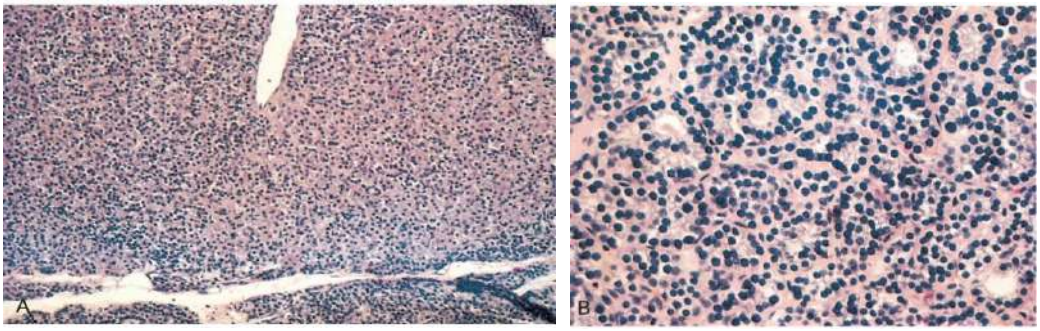


Figure 10- Chief cell parathyroid adenoma; A. Low power view B. High power view showing variation in nuclear size and tendency to form follicles with no anaplasia[32]

Genetic defects associated with hyperparathyroidism: [10]

1. Overactivity of proto-oncogenes (uncontrolled cellular growth-gain of function mutation);

2. Loss of function of Tumour Suppressor Genes

Mutations in the MEN-1 (TSG) gene locus, which encodes for the protein MENIN on chromosome 11q13, can be inherited with already one mutated allele hereditarily. Somatic cell mutation leads to mutation of the other allele, leading to monoclonal proliferation and tumour formation. However, in 15-20% presentation can be sporadic. Following Knudson's two-hit

hypothesis for neoplasia, early-onset hereditary neoplasms typically arise due to a single event. In contrast, sporadic adenomas occur at later age due to requirement of two somatic events.

A more intricate scenario arises from the bi-allelic loss of the functional copy of the HRPT2 gene (also known as CDC73), detected in 75-80% of cases of PHPT. This gene encodes the protein parafibromin and was initially identified as the cause of HPT-JT syndrome. Therefore, it is apparent that, in addition to presumed mutations in non-coding regions, genetic defects in HRPT2 are likely present in nearly all parathyroid carcinomas.

In certain parathyroid adenomas, proto-oncogene activation has been observed. In MEN-2 syndrome, activation of the RET gene initiates C-cell hyperplasia, which can progress to medullary thyroid carcinoma through clonal expansion. Additionally, a reciprocal translocation on chromosome 11 places the PTH gene promoter upstream of CCND1, which encodes cyclin D protein. This alteration leads to overexpression of CCND1 and increased cellular proliferation, observed in 20-40% of parathyroid adenomas.[10]

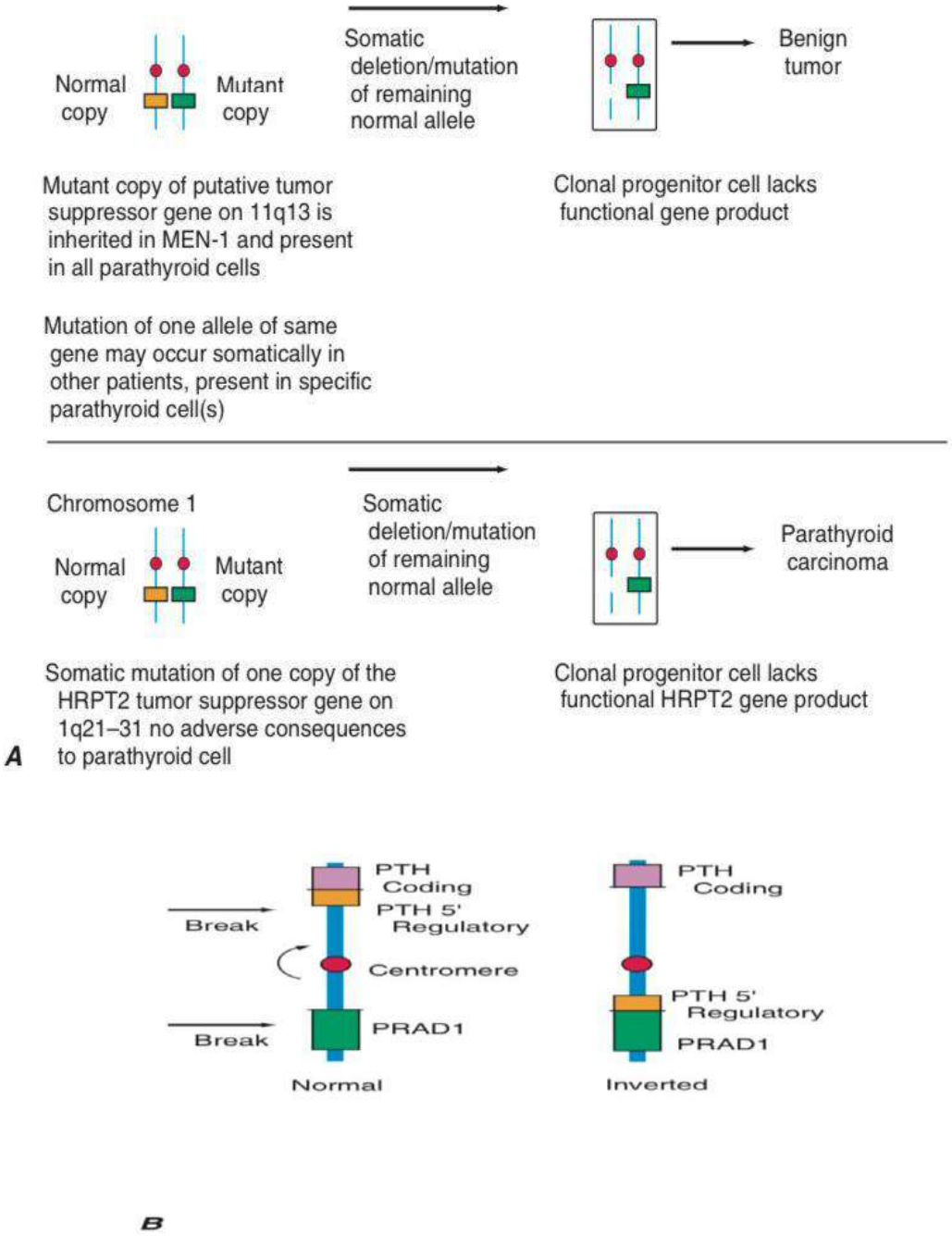

Normal copy
Mutant copy
Somatic deletion/mutation of remaining normal allele
Benign tumor
Mutant copy of putative tumor suppressor gene on 11q13 is inherited in MEN-1 and present in all parathyroid cells
Clonal progenitor cell lacks functional gene product
Mutation of one allele of same gene may occur somatically in other patients, present in specific parathyroid cell(s)
Chromosome 1
Normal copy
Mutant copy
Somatic deletion/mutation of remaining normal allele
Parathyroid carcinoma
Somatic mutation of one copy of the HRPT2 tumor suppressor gene on 1q21–31 no adverse consequences to parathyroid cell
Clonal progenitor cell lacks functional HRPT2 gene product
A
PTH Coding
PTH 5' Regulatory
Break
Centromere
PRAD1
Break
Normal
PTH Coding
PTH 5' Regulatory
PRAD1
Inverted
B

Figure 11- A. Molecular events in tumour susceptibility- growth regulatory influence of the disease is impaired leading to unregulated growth and formation of tumour. B. Mechanism and consequence of gene rearrangement leading to overexpression of PRAD-1/cyclin-D1 gene by highly active PTH gene promoter.[10]

FHH is a rare AD disorder caused due to loss of function mutation in calcium-sensing receptor gene (CaSR). This mutation leads to reduced sensitivity to extracellular calcium levels.[32]

Clinical Presentation:

Primary hyperparathyroidism is clinically defined by a set of five symptoms associated with hypercalcemia: bone issues, kidney stones, abdominal discomfort, psychological symptoms, and fatigue. In developing countries like India, PHPT often presents as a condition with noticeable symptoms. This is likely because routine screening for hypercalcemia is not widespread and access to medical facilities, especially in rural areas, is limited.[1]

Skeletal manifestations:

Skeleton is one of the most common sites involved in PHPT. Symptoms vary from bony pains to osteitis fibrosa cystica (OFC) and pathological fractures. Common dental changes are loose teeth, loss of teeth, or epulis. [1]

A. **B.1** **B.2**

Figure 12- A. showing advanced bone disease with multiple fractures, B.1 showing OFC replaced with prosthesis in humerus as shown in B.2[36]

The most sensitive and specific finding of bone involvement in PHPT is subperiosteal resorption of long cortical bones. Cortical long bone involvement is more frequent and severe as compared to cancellous bone. Rare palpable brown tumours can be elicited on examination. In recent years OFC has been very rare presentation in modern days due to early diagnosis.[10] DEXA of the spine provide quantitative spinal bone density estimates. Primarily the cortical densities are estimated quantitatively by densitometry of the distal radius or hip. In PHPT, cortical bone density is decreased while cancellous bone density remains relatively preserved.[10]

Yu Wang *et al.* [37] published a rare case study documenting severe bony involvement resulting from PHPT. The report described a young male who presented with pain and limited mobility of his right arm and right hip following a trivial fall. Computed tomography revealed a supracondylar fracture of the right humerus, a fracture of the right femoral neck, and multiple brown tumors. Patient was diagnosed with PHPT based on hypercalcemia, raised PTH along with USG neck showing hypoechoic mass. Patient underwent parathyroidectomy with pathological examination revealing parathyroid adenoma. Patient followed for 6 months with symptom free appearance.

Bone mineral density is frequently and more severely reduced in symptomatic PHPT. Following parathyroidectomy bone mineral density shows a rapid, remarkable and striking recovery, often with >100% gains above baseline over months to years. Whereas average increase in BMD in asymptomatic following surgery is of the order of 15%. Even after significant rise in BMD the recovery of cortical bone density may be incomplete as compared to cancellous bone.[1]

Renal manifestations:

Kidneys are one of the common target organs involved in primary hyperparathyroidism. In India the incidence of renal disease varies from 30-60% with presence of hypercalciuria in 30-40% of the patients. Another

renal manifestation is diffuse calcium phosphate complex deposition known as nephrocalcinosis with frequency varying from 15-20%.PHPT may be associated with decreased creatinine clearance.

Misgar *et al.* conducted a study to characterize patients with PHPT who also had nephrolithiasis, comparing those with silent stones to those with symptoms. They reviewed data from more than 150 PHPT patients, categorizing them based on symptoms, history of graveluria, or any prior renal calculi. The study concluded that patients with silent renal stones exhibited significantly low calcium level with relatively higher phosphate level as compared to those with symptoms.[38] Incidence of nephrocalcinosis and nephrolithiasis is 7%, progression to renal stones is mostly reversed by parathyroidectomy. Renal insufficiency measured as decreased eGFR <60 ml/min was relatively common (17%).

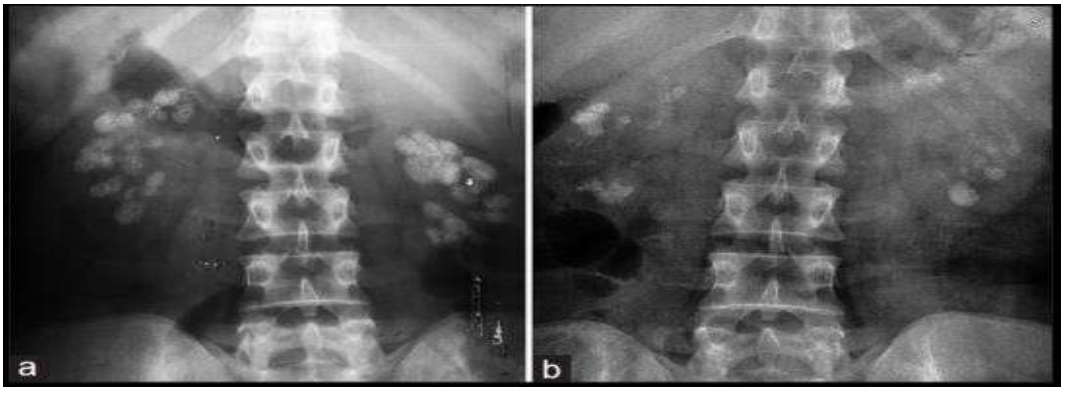


Figure 13- A. Extensive B/L nephrolithiasis B. Improvement in same patient after parathyroidectomy [38]

Abdominal groans:

Arora *et al.* published a case series involving 30 patients where acute pancreatitis was the initial manifestation of primary hyperparathyroidism. The study emphasized the importance of timely diagnosis to prevent recurrent attacks. They concluded that patients with primary hyperparathyroidism-associated pancreatitis tend to be male, had higher

calcium levels, and less frequent skeletal involvement compared to those without pancreatitis unrelated to hyperparathyroidism. The presence of nephrolithiasis was significantly linked to severe pancreatitis outcomes. One patient in the study had refractory hypercalcemia with renal involvement and was successfully treated with denosumab. Although rare, primary hyperparathyroidism presenting as acute pancreatitis requires a high level of suspicion for diagnosis, especially when normocalcemia is observed at presentation.[9]

On review of literature various studies have stated high prevalence of constipation in patients with primary hyperparathyroidism. Positive association is also seen with peptic ulcer disease in approximately 9% patients and resolution of symptoms post parathyroidectomy has been established. Also the high prevalence of gall stone disease has been documented in symptomatic PHPT.[1]

Psychic overtones:

Neuropsychiatric evaluation is a focal point of research, particularly in India. According to Goyal *et al.*[39], a wide range of psychiatric symptoms from mild personality changes to severe depression or psychosis have been observed in patients with PHPT. The study concluded that psychological distress is multifaceted and symptoms significantly improved by six weeks following parathyroidectomy. Interestingly, no correlation was found between serum calcium levels and psychiatric symptoms. In a recent study by Liu *et al.*[40], validated scales such as the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) were utilized to assess depression and anxiety. The findings indicated that patients who underwent parathyroidectomy demonstrated significant post-surgical improvement, consistent with the conclusions drawn by Chiba *et al.* [41] in 2007.

Haematological manifestations:

Haematological manifestations are common in symptomatic PHPT patients with anaemia being the most common manifestation in 30-40% patients. High prevalence of anaemia is multifactorial also includes PTH induced marrow fibrosis mediated by increased cytokines (interleukins) and TNF-α coupled with decreased EPO levels. Anaemia and fibrosis both are shown to improve after parathyroidectomy. Thrombocytopenia associated is also proposed to be due to marrow fibrosis as well.[1] Anaemia was first reported in the 1930s.[42] The prevalence of anaemia in primary hyperparathyroidism varied between 5% and 31.8% in studies conducted before the 1990s. [43-45] However, a study published in 2009 [46] reported a prevalence of up to 50 percent. In cases of primary hyperparathyroidism (PHPT), anemia typically manifests as normocytic normochromic anemia, indicative of chronic disease. Conversely, thrombocytopenia as a manifestation of PHPT was first documented in the literature by Bhadada *et al.*[47,48] in 2012, and subsequently by Keukeleire *et al.* in 2017.[49] They concluded based on various cases about association of PHPT with thrombocytopenia, such that this haematological abnormality could be considered as a component in the spectrum of factors in the decision tree for surgical management in otherwise asymptomatic individuals.

Russo *et al.*[50] in their study have shown that serum intact PTH level of >120.5 pg/ml is strongly associated with haemoglobin level of < 10 g/dl. Nevertheless, Kır *et al.*[51], in a recent study from 2022, concluded that the development of anemia can occur irrespective of the levels of PTH in patients with PHPT.

The disease is linked to several adverse cardiovascular outcomes, believed to be caused by heightened systemic inflammation. In 2018, Lam *et al.*[52] conducted a study to examine longitudinal changes in neutrophil-to-lymphocyte ratio (NLR) before and after surgical intervention. Their

findings indicated a positive correlation between NLR and serum calcium as well as PTH levels, suggesting an association between PHPT and systemic inflammation.

Cardiovascular manifestations:

Purra *et al.* in 2022 in a study concluded that symptomatic PHPT patients tend to have substantial cardiac structural as well as functional abnormalities including elevated LVMI, diastolic dysfunction, and valvular, septal and myocardial calcium depositions. The study strongly suggested to include cardiovascular assessment in the form of 2D ECHO in patients with PHPT to detect subclinical cardiac dysfunction.[53] Devereux *et al.* [54] established an echocardiographic method to calculate LVM based on left ventricular internal dimension (LVID), posterior wall thickness (PWT), and interventricular septal thickness (IVST). This method excludes the thickness of endocardial echo lines from the measurement of PWT, while including the thickness of endocardial echo lines of the left septum and posterior wall in LVID. Study concluded calculation as Formula 1.

Systolic dysfunction- As a determinant of systolic function FS (fractional shortening) (Formula 2) and EF (ejection fraction) (Formula 3).

Diastolic dysfunction: The peak of early diastolic velocity (Emax) represents early rapid filling of LV whereas Amax depicts late peak diastolic velocity and is the measure of atrial contraction. E/Amax is widely used as marker of diastolic dysfunction. But this index should be assessed with reference to age specific values as there is physiological decline in ratio with age progression.(Spirito and Maron echocardiographic score)[55]

Measurement of QT interval: The QT interval is defined as the duration from the beginning of the Q wave to the end of the T wave on ECG. Variation of QT with cycle length is taken into account and corrected QT is determined most commonly using Bezett's formula [56]

Formula 1- Anatomic LVM = 0.8 {1.04 ([LVID + PWT + IVST] ^{3} - [LVID] ^{3})} +0.6 g (*taking LV dimension in cm)*

Formula 2- FS= [(LVEDD-LVESD) x 100]/LVEDD

Formula 3- EF= [(LVEDD^3-LVESD^3) X 100]/LVEDD^3

Formula 4- QTc=QT/RR$^{1/2}$ {Bezett's formula [56]}

Figure 14- Formula index used in cardiovascular assessment

On review of literature studies have consistently determined that PHPT does not affect systolic functions [57, 58]. For the diastolic dysfunction mostly studies have reported high incidence of impaired filling in patients with PHPT. However Piovesan *et al.*[58] suggested normal LV inflow indices. PTH induced deficit in mitochondrial energy production leads to decreased early rapid filling leading to decreased E max while late filling phase tend to be affected by myocardial calcifications. High incidence of LVH results from direct trophic effect of PTH on myocytes.[59]Also LVH can be attributed to systemic hypertension which tends to occur due to arterial intimal and medial calcification[60].PTH can also has direct influence on blood pressure and 40-50% PHPT patients have been reported to be hypertensives.[58]

Rare presentations:

Yun Xu *et al.* [61] reported a case of a 31-year-old pregnant patient in her second trimester who presented with a brown tumour in her left lower leg. This condition was attributed to a hypercalcemic crisis caused by primary hyperparathyroidism due to a parathyroid adenoma. The patient required continuous renal replacement therapy to lower her ionized calcium levels. Parathyroidectomy was performed during the 19th week of pregnancy. Two days after the surgery, there was a threat of miscarriage, which was managed with magnesium sulphate to prevent it. Five days post-surgery, hypocalcemia occurred and was treated with calcium gluconate, calcium

carbonate, and vitamin D3. The study concluded that maternal primary hyperparathyroidism is uncommon and difficult to diagnose, posing potentially life-threatening complications for both mother and fetus. Deciding on surgery for a pregnant woman with this condition is more complex compared to men or non-pregnant women.

In normal pregnancy due to changes in calcium homeostasis the serum calcium is maintained in relatively lower range. The factors responsible for lower calcium levels include hemodilution, hypoalbuminemia, hypercalciuria resulting due to raised eGFR, trans-placental calcium transport to foetus. Also, the raised oestrogen levels in pregnancy inhibit PTH levels. Hence high index of suspicion should be kept for pregnant females with symptoms. For diagnostic imaging 99mTc-sestamibi is contraindicated, and safest modality is USG-neck.

Serious maternal and foetal complications can occur. Maternal complications include renal stone disease, pancreatitis, hyperemesis gravidarum, pre-eclampsia, eclampsia and altered sensorium. There is high risk of hypercalcemic crisis which can be a life threatening with high risk of coma or even death. Very high rate of foetal complications (upto 80%) has been seen in patients with untreated PHPT. Foetal complications may include IUGR, neonatal tetany or even neonatal demise.[3]

Maternal hypercalcemia leads to trans-placental excessive efflux into foetal circulation which leads to neonatal parathyroid gland suppression which leads to transient neonatal hypoparathyroidism which can progress to fatal neonatal tetany.

For treatment in mild-moderate cases conservative management is preferred however in severe cases surgical intervention is definitive option. If surgery is required according to severity then second trimester

is most appropriate time as organogenesis is complete and risk of anaesthesia leading preterm delivery is the least.[1]

Kar *et al.* [62] in 2003 reported unusual patient of parathyroid carcinoma who without any local recurrence presented with cerebral and pulmonary metastasis. Also special reference to acute life threatening complications of PHPT was given by Kistler *et al.* [63], who in a study analysed 152 patients. It was stated that mortality of cases with acute parathyroid crisis is 52.5%.

Data from SGPGIMS [36] in India showed that 57% of patients had fractures, 49% had brown tumors, and 27% were significantly impaired due to multiple fractures. Additionally, 36% of patients had both bone and kidney disease and 38% exhibited psychiatric symptom. Bhansali *et al.* [64], reported similar findings: bony (67%), fractures (48%), renal calculi (21%), psychiatric symptoms (23%) and peptic ulcers (15%).

Patients with PHPT tend to have higher incidence and prevalence of comorbidities including DM, HTN, CAD and CVA due to prolonged systemic inflammatory status. A prospective study at two centres was done by Celik *et al.* [65] in 2017 to examine whether PTH and vitamin-D levels, together or separately, indicate the risk of stroke. It was concluded that both PTH and vitamin D appeared to be separate risk factors for CVA. Vitamin-D level was the most powerful marker for the predicting the stroke risk. Both PTH and vitamin-D should be assessed in conjunction for accurate determination of risk of stroke. In another study by Taylor *et al.* [66] it was concluded that approximately 40% of patients with PHPT have impaired glucose tolerance. Insulin resistance probably arises from a raised intracellular free calcium levels. If left untreated it further increases the risk of other comorbidities like HTN.

Table 2- Summary of clinical features of PHPT divided as classical and non-classical features [67]

<table>
<tr><th colspan="4">Classical PHPT symptoms</th></tr>
<tr><th colspan="2">Renal</th><th colspan="2">Skeletal</th></tr>
<tr><td colspan="2">• Polyuria
• Nephrolithiasis
• Nephrocalcinosis
• Impaired renal functions</td><td colspan="2">• Bony pains
• Osteoporosis
• Pseudogout
• Fractures
• OFC
• Brown Tumors</td></tr>
<tr><th colspan="4">Non Classical PHPT symptoms</th></tr>
<tr><th>Gastrointestinal</th><th>Cardiovascular</th><th>Neuromuscular</th><th>Neurobehavioral</th></tr>
<tr><td>• Anorexia
• Abdominal pain
• Nausea
• Vomiting
• Constipation
• PUD
• Cholelithiasis
• Pancreatitis</td><td>• Arrhythmias
• HTN
• LVH
• VPC</td><td>• Weakness
• Fatigue
• Cramps
• Proximal muscle atrophy</td><td>• Depression
• Anxiety
• Irritability
• Altered mental status
• Dementia
• Sleep disturbance</td></tr>
</table>

Diagnostic work-up:

In the resource-rich systems most of the patients are incidentally identified in the asymptomatic phase usually due to routine serum calcium level measurements. However in the developing countries cases are mostly identified in symptomatic phase, e.g. with renal calculi or multiple fractures. The combination of elevated corrected serum calcium levels (Formula-5) and high/inappropriate high PTH is the key to diagnosis of PHPT [68, 69].

Formula-5 (Albumin adjusted)

Corrected calcium (mmol/L) = total calcium (mmol/L) + 0.8 [4 – albumin (g/L)]

Figure 15 – Formula used to calculate albumin adjusted serum calcium levels [70]

Differential diagnosis-When in a patient both calcium and PTH are elevated (or inappropriately high) before concluding the diagnosis of PHPT we need to rule out various drugs like thiazides[71] being widely used as antihypertensive agents worldwide which can lead to hypercalcemia probably due to inhibition of TRPV5 and increased calcium reabsorption due to volume depletion [72,73]. Lithium is another drug that interacts with the calcium-sensing receptor (CaSR) which leads to set point elevation of calcium concentration [74]. Lithium discontinuation can lead to calcium normalization.

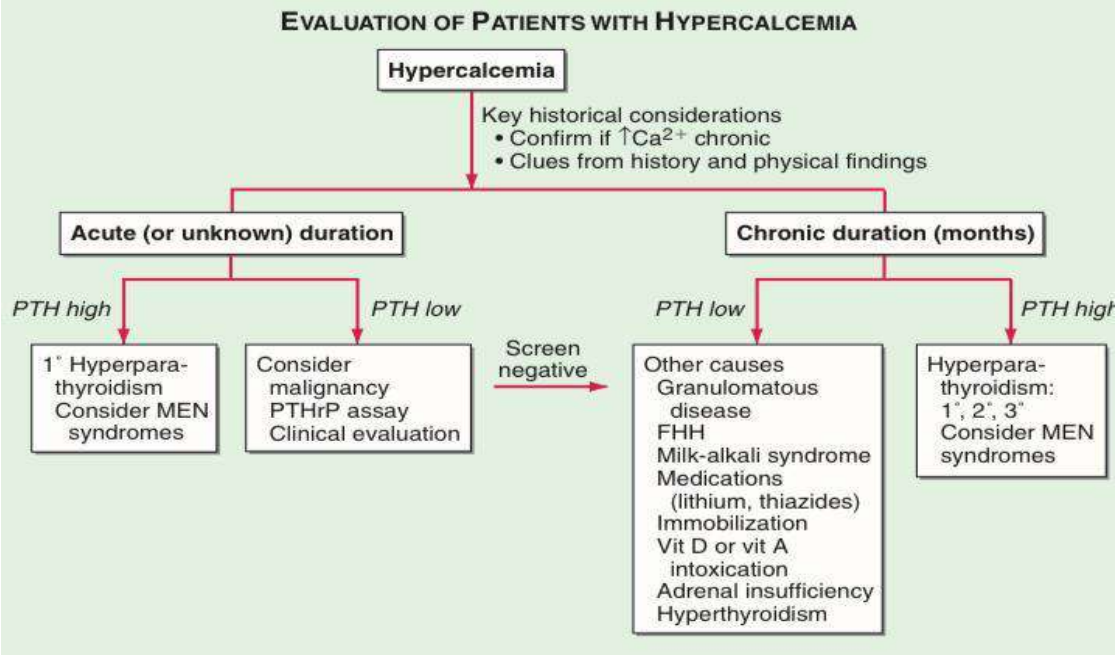

EVALUATION OF PATIENTS WITH HYPERCALCEMIA
Hypercalcemia
Key historical considerations
• Confirm if ↑Ca2+ chronic
• Clues from history and physical findings
Acute (or unknown) duration
Chronic duration (months)
PTH high
PTH low
PTH low
PTH high
1° Hyperpara-thyroidism Consider MEN syndromes
Consider malignancy PTHrP assay Clinical evaluation
Screen negative
Other causes Granulomatous disease FHH Milk-alkali syndrome Medications (lithium, thiazides) Immobilization Vit D or vit A intoxication Adrenal insufficiency Hyperthyroidism
Hyperpara-thyroidism: 1°, 2°, 3° Consider MEN syndromes

Figure 16 - Evaluation of patients with hypercalcemia [10]

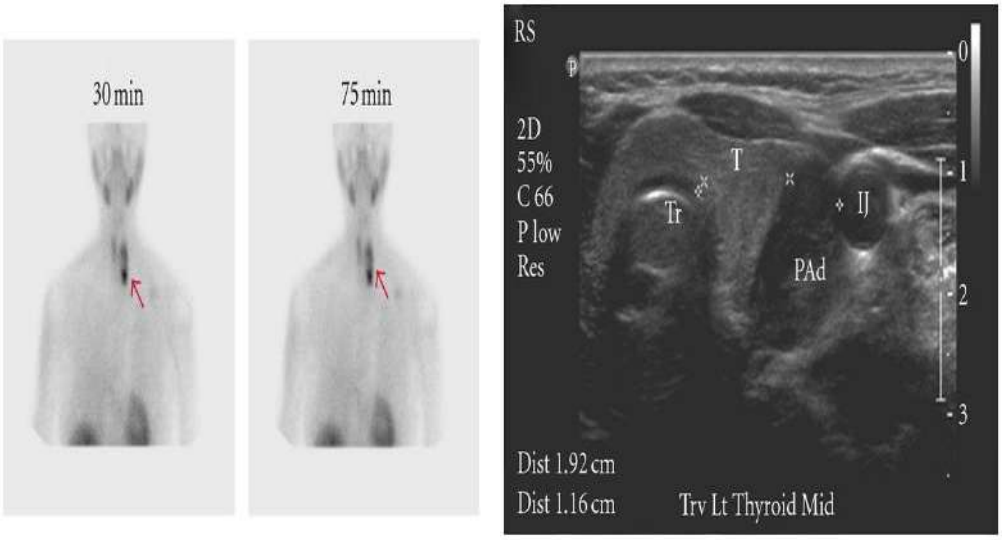
Preoperative radiological investigations

USG is one of the most common imaging methods used due to its low cost, non-invasive nature and no exposure to ionizing radiations [75]. Cheung *et al.*[76] conducted a meta-analysis of studies published from 1997 to 2009. The analysis revealed that ultrasound (USG) had an average sensitivity of 76% (ranging from 43% to 96%) and a PPV of 93% in patients with PHPT. The presence of multiglandular disease or concurrent thyroid conditions such as goitre and thyroid nodules was associated with decreased sensitivity of USG. Ultrasound has limited value in the evaluation of retroesophageal lesions due to the inability to penetrate the clavicles or sternum.[77]

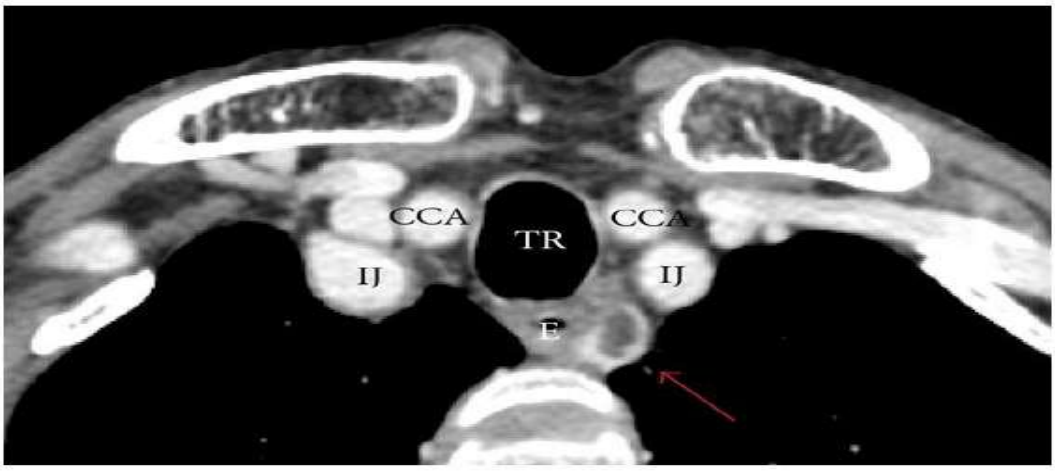
Scintigraphy was initially introduced as 99mTechnetium-multiplex ion-beam imaging by Coakley *et al.* in 1989 [78]. Their research revealed that sestamibi, a lipophilic cation, tends to accumulate predominantly in mitochondria, particularly in the thyroid and parathyroid glands, as well as in salivary glands and cardiac muscle cells. During scintigraphy, the

maximum thyroid activity is typically observed within five minutes following injection of sestamibi. However, parathyroid washout is delayed because of which adenoma remains visible even after a delayed period of two hours [79].Newer modality of double-tracer scintigraphy was later invented, in which a thyroid-specific isotope ^{99m} Tc-pertechnetate or ^{123} Iodine was used together with ^{99m} Tc-MIBI. The double-tracer method has been shown to have higher sensitivity compared to using 99mTc-MIBI alone (72–94% versus 62–79%).[80]

Localization of the multiglandular adenoma is challenging. Ruda *et al.*[81] reviewed findings from 215 studies and determined that imaging sensitivity is 88% for a single adenoma, 45% for multiglandular adenomas, and 30% for double adenomas. SPECT when combined with CT, provides a three-dimensional image of the lesion, offering even more precise anatomical localization. According to a recent study [82], 99mTc-MIBI SPECT/CT has been identified as the preferred imaging modality. However, dual-phase 99mTc-MIBI SPECT/CT is more costly (241% of the cost of planar imaging) and exposes patients to higher radiation levels. Patients with negative scintigraphy for parathyroid tumors typically have a predominance of chief cells, whereas those with positive results more often exhibit oncocytic cells. Oncocytic cells, which have higher mitochondrial content, tend to show positive findings on scintigraphy. A multi-centric Scandinavian study reported a significant surgical failure rate of up to 17% in patients with negative findings on both ultrasound and scintigraphy.[83]



(a) (b)



(c)

Figure 17- Radiological imaging in PHPT (a) Sestamibi SPECT (b) Cervical ultrasound (c) 4D-CT scan(ectopic parathyroid adenoma) [78]

Treatment

Treatment of choice for PHPT is surgical resection. To buy time for surgery medical management is given especially in moderate to severe hypercalcemia (>12 mg/dl).[1] Patients with primary hyperparathyroidism (PHPT) who decline surgery are monitored annually, checking serum calcium levels and estimated GFR. If renal involvement is suspected or symptoms of kidney stones are present, renal imaging (ultrasound) and a 24-hour urine calcium test are advised [84]. All the unoperated patients should be supplemented cautiously with vitamin D to increase the serum Vitamin D3 level and maintain between the range 50 and 75 nmol/l [85]. The recommended initial dose for Vitamin D3 supplementation is 600–1000 IU of cholecalciferol daily. An interventional study by Rolighed *et al.* demonstrated that even a daily dose of 2800 IU could be used safely. This dosage effectively reduces PTH levels and decreases bone resorption without significantly affecting serum or urinary calcium levels. [86].

Pharmacological intervention

Pharmacological treatments may be appropriate for those with low bone mineral density (BMD), individuals who qualify for surgery but are not candidates due to comorbidities, or those who decline surgery. Additionally, pharmacological intervention can be considered for patients with familial PHPT or for those experiencing persistent or recurrent hypercalcemia after surgical treatment.[87]

- Hydration with forced diuresis

Hypercalcemic patients tend to be dehydrated due to vomiting or polyuria. On restoration of normal hydration serum calcium starts decreasing within hours. Hydration should be titrated by CVP and serum electrolytes monitoring. In severe life-threatening hypercalcemia upto 4-6 l of isotonic saline with furosemide upto 100 mg every 1-2 hours may be required.

- Oestrogen

Long-term hormone replacement therapy (HRT) in postmenopausal women is considered a valuable option for protecting bone health. A four-year extension study conducted with 23 patients found that those treated daily with 0.625 mg of conjugated equine oestrogen and 5 mg of medroxyprogesterone acetate experienced increased bone mineral density (BMD). On follow-up of serum calcium, from 1-2 year levels were almost of static but slightly lower in 4-year extension study.[88]

- SERMS

In a 12 month RCT comparing efficacy of raloxifene and alendronate in 24 patients it was demonstrated that there were significant beneficial effects on spine, however similar results were not replicated at femoral neck or other radial sites. [89]. A shorter randomized controlled trial involving 18 postmenopausal women demonstrated a significant decrease in serum calcium and bone turnover markers. However, there were no changes in serum PTH, ALP, or urinary calcium excretion.[90]

- Aminobisphosphonates

Aminobisphosphonates are the class of antiresorptive drugs which inhibit osteoclastic action. Seven short-term studies have reported on the use of pamidronate with significant serum calcium level reduction. However no data for BMD was available in these due probably due to short term follow-up. Five of seven studies also reported transient increase in serum PTH levels.[87]Twelve studies have reported on the use of Alendronate in PHPT, with majority studies having long term data of ≥48 weeks. Significant initial decrease in serum calcium has been reported lasting for more than 6 months.[87]

The largest double-blinded randomized controlled trial (RCT) evaluated the effects of a daily 10 mg dose of alendronate over one year. This study

included more than 40 PHPT patients who either did not meet the criteria for surgery or refused it. By the end of the study, there was a significant increase in bone mineral density (BMD) from baseline. Although serum, urine calcium levels and PTH remained unchanged, there was a significant decrease in bone turnover markers.[91]

- Denosumab

Denosumab is an antiresorptive human monoclonal antibody which blocks RANKL binding leading to inhibition of osteoclast development and activity. A retrospective longitudinal study conducted in 2018 demonstrated the beneficial effects of treatment on bony protection in patients with osteoporosis. After 1-2 year of therapy significant increase in BMD, decrease in ALP levels has been reported. However it has not shown decrease in serum calcium levels.[92]

- Cinacalcet

Cinacalcet, a calcimimetic agent, is approved for the treatment of hyperparathyroidism in the European Union (2004).Cinacalcet is also approved in the Canada and USA for unoperated PHPT, as treatment of secondary HPT in dialysis patients. Cinacalcet increase the sensitivity of the calcium-sensing receptor to the stimulation by extracellular calcium. It leads to decreased synthesis followed by decreased secretion of PTH, ultimately leading to decreased serum calcium levels.[93] 28 studies regarding the usage of Cinacalcet in PHPT were combined in a recent systematic review and meta-regression which concluded that serum calcium and PTH levels were significantly reduced with normalization in 90% participants across the studies. Although no effect on BMD was reported hence no skeletal protective effect could be ascertained.[94]

- Calcitonin

Human and salmon hormone as calcitonin are available which inhibit osteoclastic bone resorption and promotes calciuresis. It has a very rapid hypocalcemic action starting in 2 hours and lasts for about 1 week.

Specimen pathology-

On review of literature pathological specimen weight has been reported differently especially in Indian and western studies. In developed countries, the average tumour weight typically ranges from 2 to 4 grams. However, among Indian patients, tumour weights have been reported to range from 1.25 to 102 grams [95]. The prevalence rates are 89.1% for adenoma, 6.56% for hyperplasia, and 4.37% for carcinoma [96]. The incidence of parathyroid carcinoma causing primary hyperparathyroidism (PHPT) in various studies ranges from 2.6% to 6%, which is higher compared to developed countries. (1%).[97]

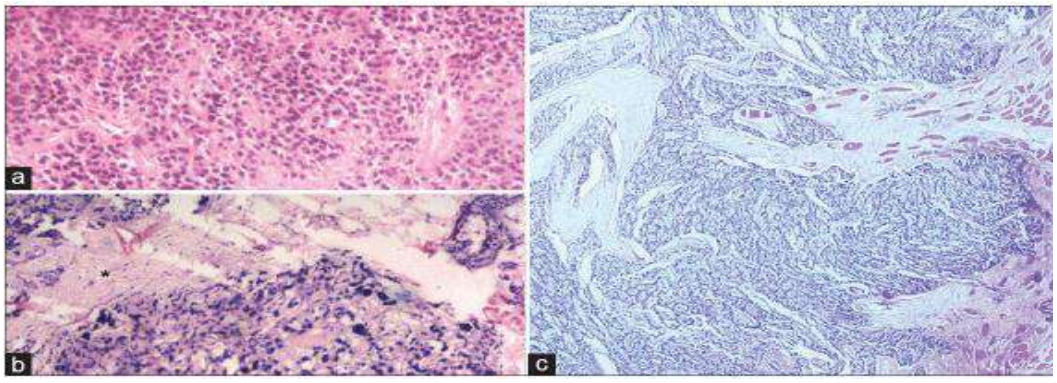


Figure 18- a) Typical adenoma with chief cells and monomorphic nuclei and absence of fat b)Atypical adenoma showing bizarre cells with prominent nuclear atypia and fibrous bands (*) c) Tumour cells with invasion beyond the capsule into skeletal muscle (■) [98]

Prognosis

Asymptomatic PHPT does not have increased mortality risk, however symptomatic PHPT is associated with significantly increased mortality and morbidity. There is speculation that the Indian population experiences more symptoms possibly due to concurrent hypovitaminosis D.[99]

At present, it is evident that the majority of patients diagnosed with the disease in India exhibit symptomatic disease. Elevated levels of calcium, PTH, and ALP are typical, often accompanied by low vitamin D levels, which exacerbate bone disease severity. Hungry bone syndrome (HBS) following surgery leads to extended hospital stays, leading to increased morbidity.

Early detection of mild and asymptomatic PHPT could significantly benefit patients if greater efforts are made to identify these cases. This requires incorporating calcium screening into routine health check-ups. The growing awareness of parathyroid disorders among physicians, reflected in the increasing number of publications on PHPT, will facilitate earlier diagnosis and management of more cases.

MATERIAL & METHODS

Source of Data

This prospective cross sectional observational study was conducted at DMCH Ludhiana between 15th September 2022 and 31st December 2023. Study group included the patients admitted in the hospital or presenting to OPD. In the 18 months years duration 128 study participants were enrolled and were followed up one time between 1-6 months duration.

METHOD OF COLLECTION OF DATA

Selection criteria

Inclusion Criteria

All patients with atleast one corrected serum calcium level of >10.2 mg/dl with PTH levels >20 ng /dl.

Exclusion criteria

1. Serum Creatinine >2.5 with evidence of chronic kidney disease (ruled out secondary primary hyperparathyroidism)
2. Kidney transplant patients or recipients of cyclosporine, tacrolimus and sirolimus (ruled out tertiary hyperparathyroidism)
3. History of invasive carcinoma.

Methodology

- All the study participants after obtaining informed consent were subjected to the various data collection methods. Detailed history regarding symptomatology and duration of symptoms prior to diagnosis was obtained. Any prior comorbidities were noted in the form of HTN, Diabetes, CAD and CVA. Local and CNS examination of patients was done. Jaw swelling and muscle power was noted.

- Grading criteria used for muscle power assessment (MRC grading)-

Grade 0- No contraction

Grade 1- Flicker or trace of contraction

Grade 2- Active movement with gravity eliminated

Grade 3- Active movement against gravity

Grade 4- Active movement against gravity and resistance. (Subnormal)

Grade 5- Normal power

- For the assessment of mental impairment MMSE was done. Data was collected according to the questionnaire and the score was calculated. MMSE score was analysed as-

30-24= No impairment (Normal)

19-23= Mild impairment

10-18= Moderate impairment

<10 = Severe impairment

- For the assessment of psychological distress PHQ-4 scoring system was used. Data was collected according to the questionnaire and the score was calculated.

On the basis of score calculated psychological distress was analysed as-

0-2= None psychological distress

3-5= Mild psychological distress

6-8= Moderate psychological distress

9-12= Severe psychological distress

Blood samples of the study participants obtained by venipuncture were subjected to routine investigations (CBC, RFT, LFT) with special interest to serum calcium, serum PTH, serum ALP, serum vitamin-D and serum uric acid levels. Urine examination was done with special interest to 24 hour urinary calcium.

Albumin corrected serum calcium levels was calculated using the formula-5: Corrected calcium (mmol/L) = Patient calcium (mmol/L) + 0.8 [4 – albumin (g/L)]

- Cardiological assessment in the study participants was done with ECG (N=103) and 2D-ECHO (N=87). To assess hypercalcemic changes in ECG special note of heart rate and QTc interval was made.

✓ In 2D ECHO systolic dysfunction was assessed by EF and FS.

✓ For diastolic dysfunction E/A ratio was calculated and if <0.8 was considered as diastolic dysfunction.

✓ PASP value was noted in the ECHO and the pulmonary hypertension was graded as-

PASP 31-45 mmHg =Mild PH

PASP 46-60 mmHg = Moderate PH

PASP >60 mmHg = Severe PH

✓ For assessment of LVH (Left Ventricular Hypertrophy) =LVMI (Left Ventricular Mass Index) was calculated as-

Anatomic LVM (Left Ventricular Mass)

= 0.8 {1.04 ([LVID + PWT + IVST]^3 - [LVID]^3)} +0.6 g (LV dimension in cm) where LVID is the left ventricular internal diameter, PWT is the posterior wall thickness and IVST is the interventricular septal thickness. LVID, PWT and IVST values were obtained from echocardiographic studies.

LVMI= LVM/ BSA (Body surface area was taken as 1.7 m2).

- ✓ Aortic value calcifications were noted and were considered as marker of ectopic calcification in echocardiographic studies.

- Further the patients were subjected to radiological assessment. USG-Neck (N=121) and Tc-99 sestamibi spect (N=117) was done to localize the adenoma lesion. In some participants where lesion was not localized were subjected to CT- neck, MRI- Neck or PET-CT. Patients also underwent X-ray B/L hand and wrist, skull or spine (N=94) and USG- whole abdomen to analysed the other associated findings like pancreatitis or renal calculi.
- Further the various medical treatment options provided to the study participants were noted. The number of days to serum calcium normalization after hospitalization, after zoledronate or after denosumab was noted.
- The data about the surgically operated patients with incidence of post-operative HBS, their histopathological analysis was noted.
- In our study the patients were followed up atleast once between 1-6 months and their serum calcium and PTH levels were noted.

Outcome

This study aimed to evaluate the clinical profile of patients presenting with PHPT. The various common or uncommon index presentations with certain biochemical variations were highlighted. Moreover the outcome with different management strategies were also assessed according to time taken to normalise calcium post drug administration. The study has helped in lowering our threshold for disease suspicion which helped in early diagnosis and decreasing patient morbidity.

Statistical analysis

The various statistical tests were used on the data collected. For observations data was categorised on the basis of gender into the male participants and the female participants. Categorical data was presented as proportions or percentages. Continuous data was presented as mean ± SD or in non-normal data distribution as median (interquartile range) as Q2 (Q1, Q3). Categorical data was compared using Chi-square test and continuous data was compared using unpaired t-test. A probability value of <0.05 was considered significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATIONS & RESULTS

The study entitled "To study the clinical profile of patients presenting with primary hyperparathyroidism" was conducted on the primary collected data. Overall, 128 clinically diagnosed PHPT patients were included. It was a prospective, cross-sectional and an observational study. The previous chapter discussed the research design, and sample selection, as well as an overview of the statistical analysis and data-collecting procedures. After data collection, under the context of the current study's goals, data was categorized, tabulated, and statistically examined. Results and their interpretations are the focus of this chapter. All of the findings have been compiled as relevant tables and are shown through graphs and placed at the appropriate location. To present results in a scientific and orderly manner, this chapter is separated into five sections:

1. Demographic data

2. Clinical presentation and examination

3. Investigational assessment

4. Treatment

5. Follow-up

1. Demographic data:

In our study the total of 128 patients of primary hyperparathyroidism were enrolled. The enrolled patients had 81 female participants (63.3%) and 47 male participants (36.7%).Male to female ratio of our study population was 1:1.7(M: F; 1:1.7).Female gender was accounting to more than 2/3rd of the study participants.

Table 3 –Tabular representation of gender-based distribution of study participants

Gender	No. of participants	Percentage
Male	47	36.7
Female	81	63.3
Total	**128**	**100**

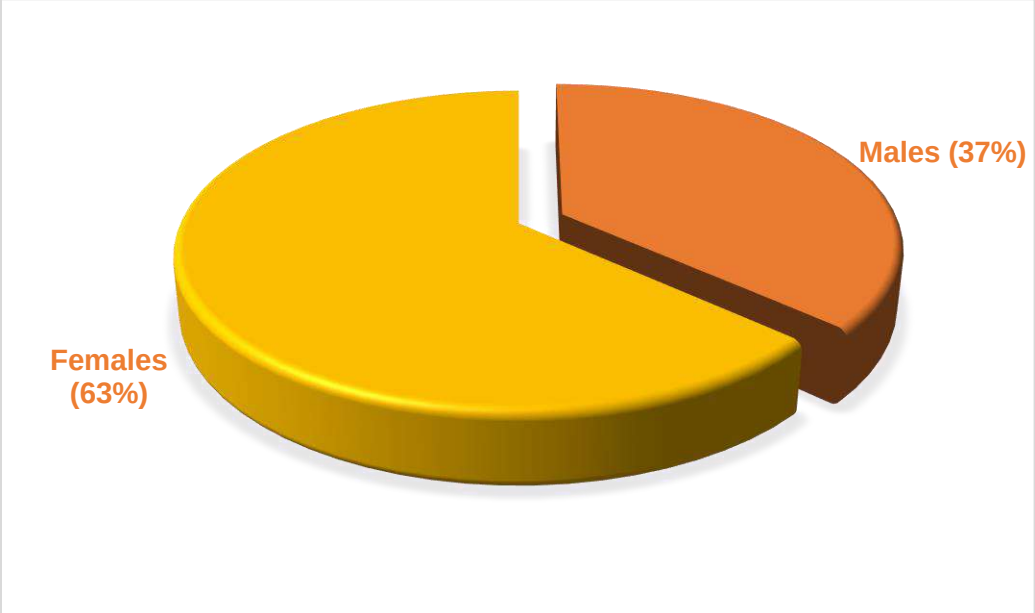


Figure 19- Pictorial representation of gender-based distribution of study participants.

Table 4- The distribution of study participants according to age groups

Age category (years)	Male n (%)	Female n (%)	Overall n (%)
11-20	1(2.1)	0(0)	1(0.8)
21-30	7(14.9)	1(1.2)	8(6.3)
31-40	10(21.3)	12(14.8)	22(17.2)
41-50	7(14.9)	14(17.3)	21(16.4)
51-60	6(12.8)	23(28)	29(22)
61-70	10(21.3)	22(27.2)	32(25)
71-80	6(12.8)	8(9.9)	14(10.9)
>80	0(0.0)	1(1.2)	1(0.07)
Total	**47(100)**	**81(100)**	**128(100)**
Mean±SD(y)	**49.6±16.7**	**55.5±12.1**	**53.3±14.2**

In our study enrolling 128 patients the age at diagnosis of the disease was noted. The overall mean age of participants at diagnosis was 53.3±14.2 years. The mean age at diagnosis amongst females (55.5±12.1 years) was more than the mean age at diagnosis amongst males (49.6±16.7 years).

The age range of patients was 19-82 years. In the age group of 11-20 years 1 male participant and nil female participant presented for diagnosis. In the age group of 21-30 years 7 male participants (14.9%) and 1 female participant (1.2%) were seen. While in the age group of 31-40 years 21.3% of the male participants (n=10) and 14.8% of the female participants (n=12) were noted. In the age group of 41-50 years 7 male participants (14.9%) and 14 female participants (17.3%) were observed. Surge in the

number cases was observed in next two decades. In the age group of 51-60 years 12.8% (n=6) of the male participants and 28% (n=23) of the female participants was observed. Similarly high proportion of participants were seen in the age group of 61-70 years including 21.3% male participants (n=10) and 27.2% female participants (n=22).With further increment in age there was decline in number of cases observed. In the age group of 71-80 years 12.8% (n=6) of the male patients and 9.9% (n=8) of the female patients were noted and above 80 years only 1 female patient was observed.

It was observed that maximum number of patients were observed in the age group of more than 50 years. 46% of the male participants and 66.7% of the female participants presented at the age of more than 50 years at diagnosis. Bimodal presentation was observed amongst the male participants (31-40 years and 61-70 years). It was observed that females have relatively more elderly presentation in comparison to males. Almost 2/3rd of the female participants were above the age of 50 years. Peak age for incidence of disease was 51-70 years. Hence PHPT was observed to be the disease of elderly female preponderance.

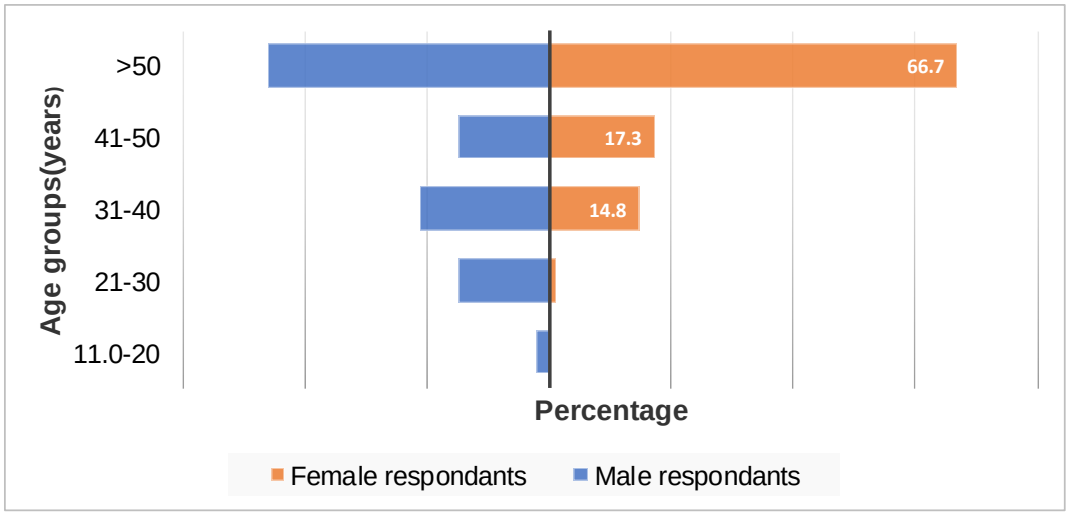


Figure 20- Pictorial representation of the distribution of study participants according to age groups

Table 5- Distribution of study subjects according to duration of illness prior to diagnosis

Duration (months)	**Male**		**Female**		**Overall**	
	n	%	n	%	n	%
0-12	15	31.9	27	33.3	42	32.8
13-24	15	31.9	18	22.2	33	25.8
25-36	4	8.5	21	25.9	25	19.5
37-48	6	12.8	10	12.3	16	12.5
49-60	4	8.5	4	4.9	8	6.3
>60	3	6.4	1	1.2	4	3.1
Total	**47**	**100**	**81**	**100**	**128**	**100**
Mean±SD (months)	**23.9±18.7**		**24.0±18.6**		**24.03±17.7**	

In our study duration of illness prior to diagnosis was observed. The overall mean duration of illness prior to diagnosis was 24.03±17.7 months. The mean duration of illness prior to diagnosis amongst males (23.9±18.7months) was similar to the mean duration of illness prior to diagnosis amongst females (24.0±18.6 months).

The range of duration of illness prior to diagnosis was 0-78 months. In our study the percentage of the male participants diagnosed within 1 year of symptom onset was 31.9% (n=15) and the female participants was 33.3% (n=27). In the duration group of 13-24 months 15 male participants (31.9%) and 18 female participants (22.2%) were seen. In the duration group of 25-36 months 8.5% (n=4) males and 25.9% (n=21) females were diagnosed. In the next span of duration from 37-48 months and 49-60 months the percentage of males diagnosed were 12.8%(n=6) and 8.5%(n=4) respectively while the percentage of females diagnosed were

12.3%(n=10) and 4.9%(n=4) respectively. However 3 male patients (6.4%) and 1 female patient (1.2%) had >5 years of symptom duration prior to diagnosis.

Hence overall it was observed that approximately 1/3rd of the study population presented within first year and more than ½ of the study participants were diagnosed within the second year of the symptom onset. However it was also observed that the females had delayed peak in duration of diagnosis from 25-36 months when compared to the males.

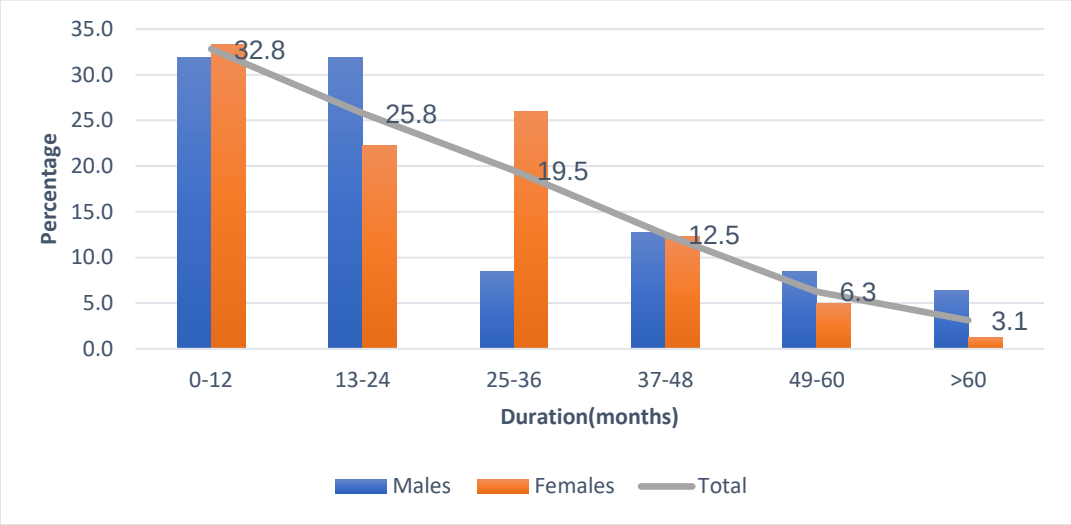


Figure 21- Pictorial representation of distribution of study subjects according to duration of illness prior to diagnosis

2. Clinical presentation and examination-

The chief complaints of the study participants were noted. In our study 128 patients were interviewed for their presenting symptoms. In our study it was observed that the most common presenting complaint was bony involvement (44.1%) followed by gastrointestinal (43.4%) and neuropsychiatric presentation (40.6%). Renal involvement was seen in 31.3% of the study participants and the patients diagnosed in the asymptomatic phase were 16.4 %.

Table 6- Tabular representation of percentage of study participants with various clinical presentations

Clinical presentation	**Male (n=47)**	**Female (n=81)**	**Overall (n=128)**
	%	%	%
Renal	34.7	29.2	31.3
Bony	38.2	47.5	44.1
Gastrointestinal	48.2	40.7	43.4
Neuropsychiatric	43.6	38.8	40.6
Asymptomatic	10.6	19.8	16.4

It was observed that amongst male participants the renal (34.7%), gastrointestinal (48.2%) and neuropsychiatric (43.6%) manifestations were more common than the female participants. On the other hand the bony involvement (38.2%) and the asymptomatic presentation (19.8%) was more common amongst the female participants.

2.1. a-Renal involvement (including renal stones, polyuria and hematuria)

Table 7-Tabular representation of number of respondents and percentage of study participants presenting with renal symptoms (renal stones, polyuria and hematuria)

Clinical presentation	**Male(n=47)**		**Female(n=81)**		**Overall(n=128)**	
	n	Percentage	n	Percentage	n	Percentage
Hematuria	14	29.8	15	18.5	29	22.7
Polyuria	22	46.8	40	49.4	62	48.4
Renal stones	13	27.7	16	19.8	29	22.7

In our study renal manifestations were noted in the form of renal stones, polyuria and hematuria. In the 47 male participants of our study the most common renal symptom was polyuria (46.8%, n=14) followed by hematuria (29.8%, n=15) and renal stones(27.7%,n=13).Similar pattern was also noted in the 81 female participants where the most common symptom observed was polyuria(49.4%, n=40) followed by renal stones (19.8%, n=16) and hematuria (18.5%, n=29). Overall polyuria (48.4%, n=62) was the most common renal symptom followed by hematuria and renal stones (both with 22.7%, n=29). It was observed that renal manifestations were more common amongst the male participants than the female participants.

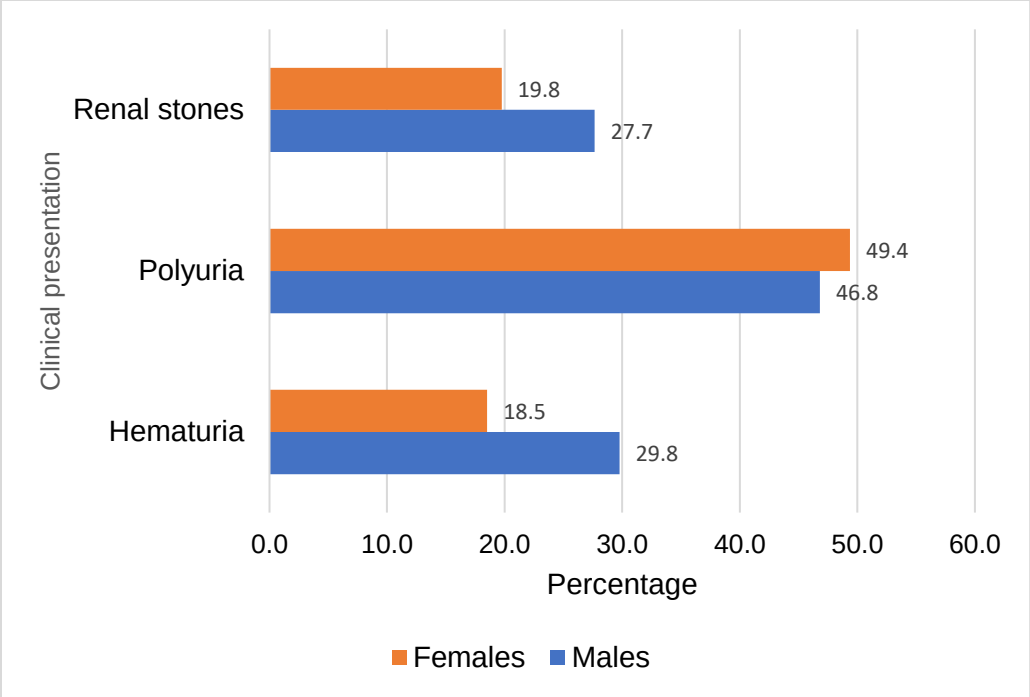


Figure 22- Pictorial representation of percentage of study participants presenting with renal symptoms (renal stones, polyuria and hematuria)

2.1. b-Bony involvement (including fractures and bony pains)

Table 8-Tabular representation of the number of study participants and percentage of study participants presenting with bony symptoms (fractures and bony pains)

Clinical presentation	**Male(n=47)**		**Female(n=81)**		**Overall (n=128)**	
	n	Percentage	n	Percentage	n	Percentage
Fractures	6	12.8	14	17.3	20	15.6
Bony pains	30	63.8	63	77.8	93	72.7

In our study bony manifestations were noted in the form of bony pains and fractures. In the 47 male participants of our study the most common bony symptom was bony pains (63.8%, n=30) followed by fractures (12.8%, n=6). Similarly amongst the 81 female participants, the most common bony symptom observed was bony pains (77.8%,n=63) followed by fractures (17.3%,n=14).Overall bony pains (72.7%, n=93) was the most common symptom followed by fractures (15.6%, n=20).

It was observed that bony pains were the most common symptom amongst both the males and the females. Also the bony involvement including both bony pains and fractures were more common in the female participants than the male participants.

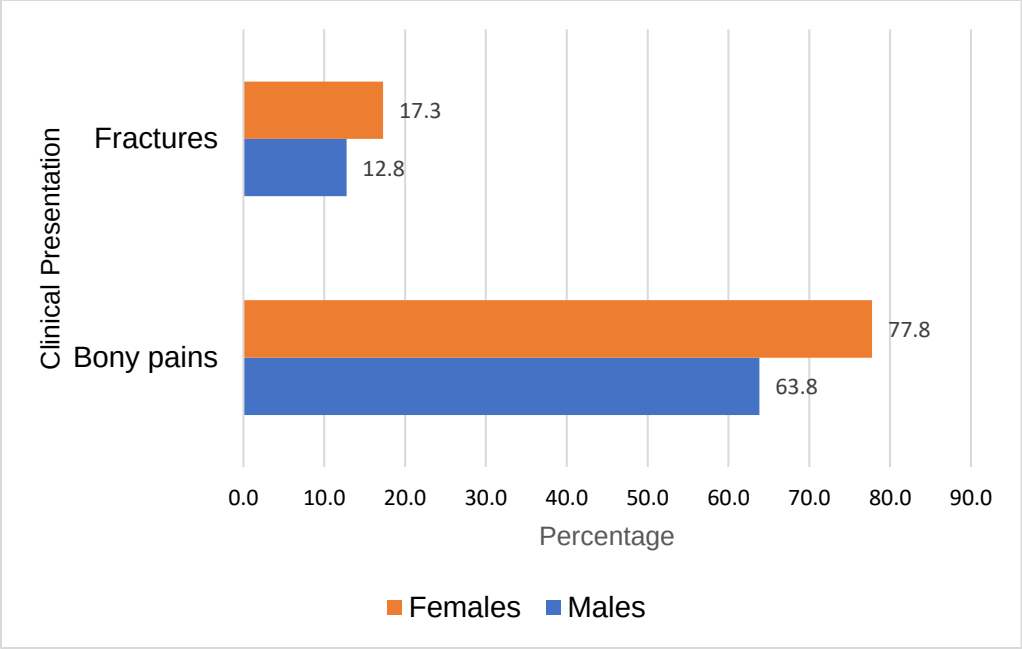


Figure 23- Pictorial representation of the percentage of study participants presenting with bony symptoms (fractures and bony pains)

2.1. c-Gastrointestinal (including pain abdomen, constipation and pancreatitis)

Table – 9 Tabular representation of number of respondents and percentage of study participants presenting with gastrointestinal symptoms (pain abdomen, constipation and pancreatitis)

Clinical presentation	**Male(n=47)**		**Female(n=81)**		**Overall (n=128)**	
	n	Percentage	n	Percentage	n	Percentage
Pancreatitis	12	25.5	15	18.5	27	21.1
Constipation	27	57.4	44	54.3	71	55.5
Pain abdomen	29	61.7	40	49.4	69	53.9

In our study gastrointestinal manifestations were noted in the form of pain abdomen, constipation and pancreatitis. In the 47 male participants of our study the most common gastrointestinal symptom was pain abdomen (61.7%, n=29), followed by constipation (57.4%, n=27) and pancreatitis (25.5%, n=12). Amongst the 81 female participants, the most common gastrointestinal manifestation was constipation (54.3%, n=44), followed by pain abdomen (49.4%, n=40) and pancreatitis (18.5%, n=15). Overall constipation (55.5%, n=71) was the most common gastrointestinal symptom followed by pain abdomen (53.9%, n=69) and pancreatitis (22.1%, n=27).

It was observed that gastrointestinal manifestations were more common in the male participants than the female participants. Higher proportion of the male participants were affected with pain abdomen and pancreatitis than the female participants.

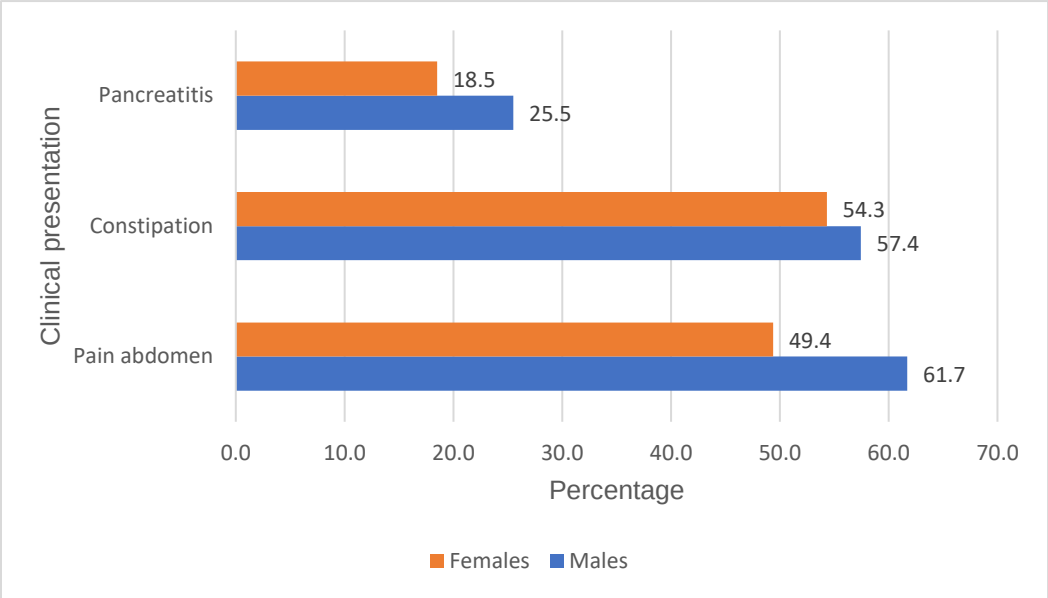


Figure 24- Pictorial representation of percentage of study participants presenting with gastrointestinal symptoms (pain abdomen, constipation and pancreatitis)

2.1. d-Neuropsychiatric (including depression and anxiety)

Table 10-Tabular representation of number of respondents and percentage of study participants presenting with neuropsychiatric symptoms (anxiety and depression)

Clinical presentation	**Male(n=47)**		**Female(n=81)**		**Overall (n=128)**	
	n	Percentage	n	Percentage	n	Percentage
Anxiety	23	48.9	31	39.5	49	38.3
Depression	18	38.3	32	38.3	55	43.0

In our study neuropsychiatric manifestations were noted in the form of anxiety and depression. In the 47 male participants of our study the most common neuropsychiatric symptom was anxiety (48.9%, n=23) followed by depression (38.3%, n=18). Amongst the 81 female participants, the most common neuropsychiatric manifestation was depression (38.3%, n=32) and anxiety (39.5%, n=31) .Overall depression (43%, n=55) was the most common neuropsychiatric symptom followed by anxiety (38.3%, n=49)

It was observed that neuropsychiatric manifestations were more common in the male participants than the female participants. Higher proportion of the male participants were affected with anxiety while higher proportion of the female participants were affected with depression.

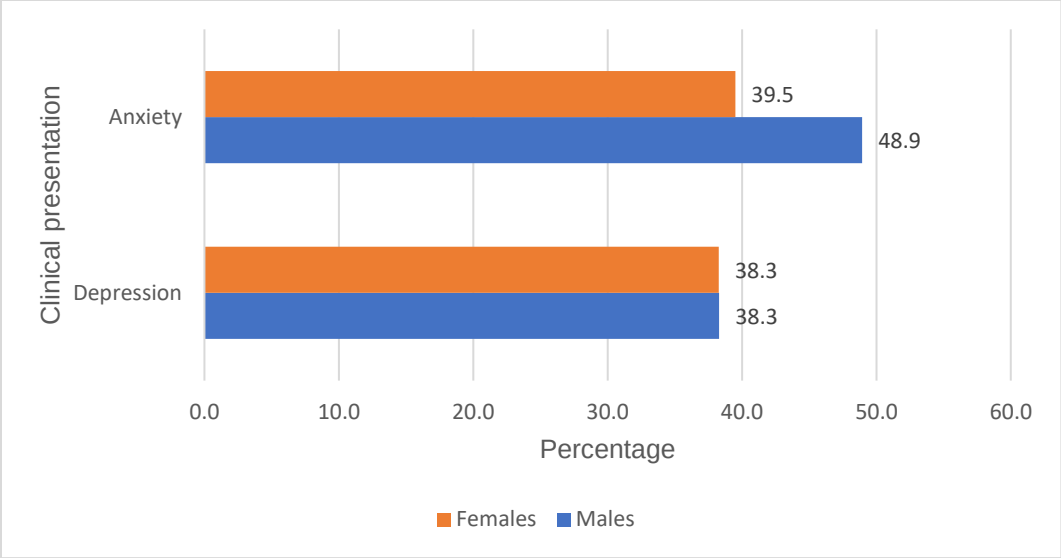


Figure 25- Pictorial representation of percentage of study participants presenting with neuropsychiatric symptoms (anxiety and depression)

2.1. e-Asymptomatic

Table 11-Tabular representation of number of respondents and percentage of study participants with no presenting complaint (asymptomatic)

Clinical presentation	Male(n=47)		Female(n=81)		Overall (n=128)	
	n	Percentage	n	Percentage	n	Percentage
Asymptomatic	5	10.6	16	19.8	21	16.4

In our study the patients presenting in asymptomatic phase were noted. Out of 47 male participants 10.6% (n=5) and out of 81 female participants 19.8% (n=16) had no symptom on presentation. Overall out of 128 patients 16.4% (n=21) were asymptomatic.

It was observed that asymptomatic presentation was more common in the female participants than the male participants.

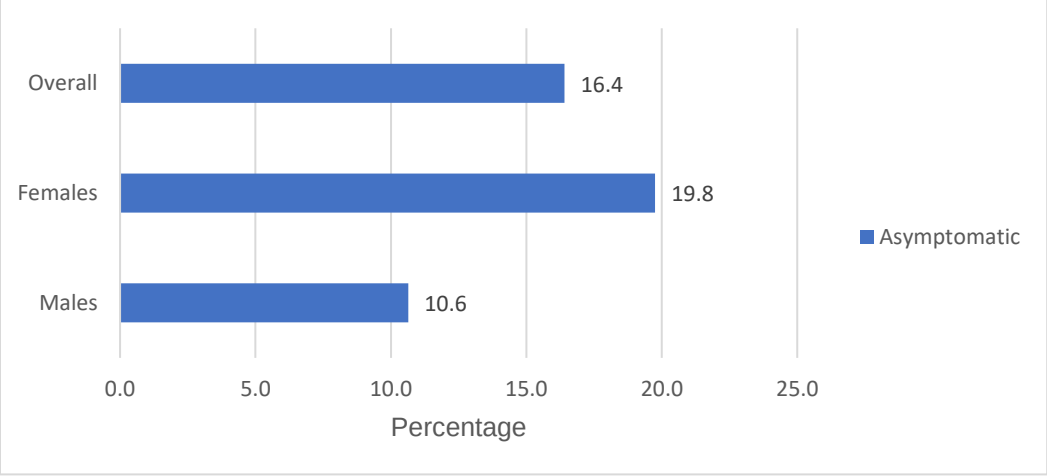


Figure 26- Pictorial representation of percentage of study participants with no presenting complaint (asymptomatic)

In our study the results and observations made according to the data collected for various clinical manifestations were shown above. For the bird's eye view the following chart was crafted for comparison of various clinical manifestations.

It was observed that amongst the male participants the list of individual symptoms in decreasing order of their prevalence was as:

1. Bony pains
2. Pain abdomen
3. Constipation
4. Anxiety
5. Polyuria

It was observed that amongst the female participants the list of individual symptoms in decreasing order of their prevalence was as:

1. Bony pains
2. Constipation
3. Pain abdomen
4. Polyuria
5. Anxiety

From the list of symptoms it was observed that the most common symptoms are the same in both the genders but their relative prevalence differs according to gender.

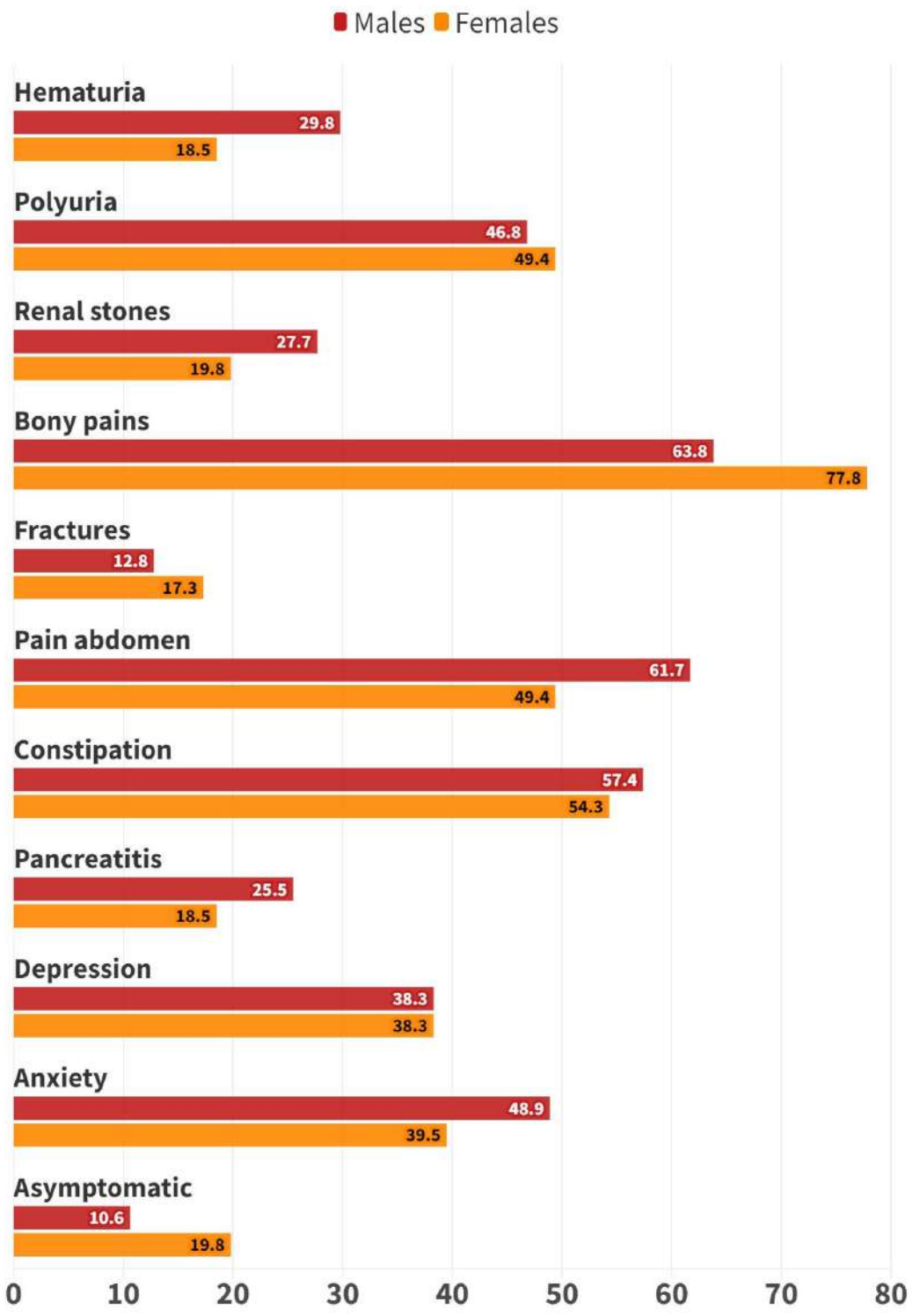


Figure 27- Pictorial representation of percentage of study participants with various clinical presentation.

Table 12-Tabular representation of chi-square and p-value analysis for various symptomatic presentations in relation to gender

Symptoms	**$\chi 2$**	**p-value**
Hematuria	2.15	0.14
Polyuria	0.07	0.78
Renal stones	1.06	0.30
Bony pains	2.91	0.08
Fractures	0.46	0.49
Pain abdomen	1.81	0.18
Constipation	0.12	0.73
Depression	0.01	0.99
Anxiety	1.07	0.29
Asymptomatic	1.8	0.18

Calcium being a very important electrolyte in the various physiological processes the multisystem involvement in PHPT could be justified. The various symptoms at presentation were explained in great detail. In an attempt to establish association between the various clinical manifestations and gender the categorical variables were subjected to chi-square test and p-values were analysed. Evident difference was observed amongst males and females on the basis of frequency and percentage analysis. But no significant association between the symptom presentation and gender was observed.

2.2 Past History

Table 13-Tabular representation of number of respondents and percentage of study participants with prior comorbidities in the form of DM, HTN, CAD and CVA

Comorbidity	n	Total %
DM	64	50
HTN	64	50
CAD	18	14.1
CVA	21	16.4

In our study the past history in the form of prior comorbidities was noted. Out of 128 study participants DM and HTN was seen in 50% (n=64) of the participants. History of CAD was noted in 14.1% (n=18) and history of CVA was noted in 16.4% (n=21). It was observed that the prevalence of comorbidities in patients with PHPT were higher than usual.

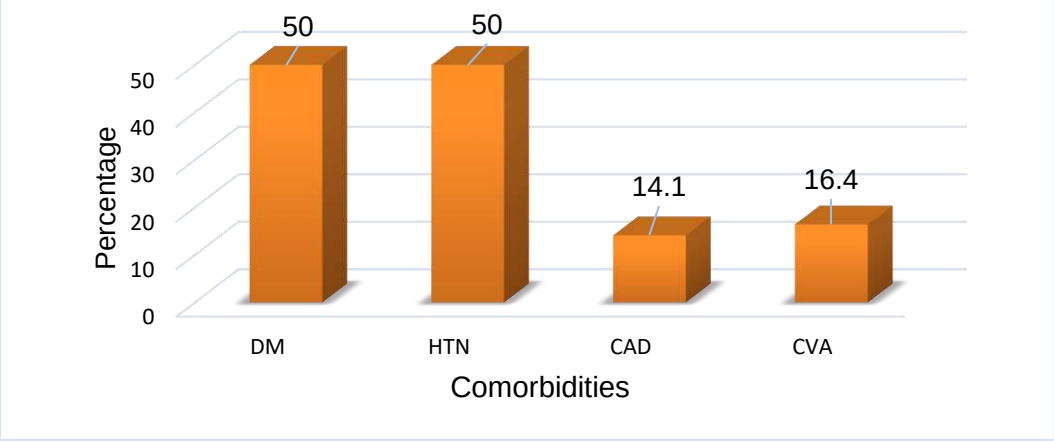


Figure 28- Pictorial representation of percentage of study participants with prior comorbidities in the form of DM, HTN, CAD and CVA

2.3 Examination:

2.3. a-General physical examination (including SBP, DBP and HR)

2.3. b-Local examination (including examination for neck mass and jaw swelling) and CNS examination (including deep tendon reflexes + muscle power)

2.3. c-Mini-mental status examination (MMSE)

2.3. d-PHQ-4 (Patient Health Questionnaire-4) assessment

2.3. a-General physical examination (including SBP, DBP and HR)

Table 14-Tabular representation of general physical examination of study participants

Variable	**Male**		**Female**	
	Mean	**SD**	**Mean**	**SD**
SBP(mmHg)	128.4	20.1	135.7	20.1
DBP(mmHg)	75.5	9.2	79	10.9
HR(bpm)	67.9	9.7	72.4	9.5

In our study the general physical examination of the study participants was noted. The male participants had the mean SBP of 128.4±20.1mmHg while mean SBP amongst the female participants was higher with the value of 135.7±20.1mmHg.

The mean DBP amongst the male participants was 75.5±9.2 mmHg and the mean DBP amongst the female participants was 79.0±10.9 mmHg. The mean HR amongst the male participants was 67.9±9.7 bpm while amongst the female participants the mean HR was 72.4±9.5 bpm.

It was observed that mean SBP in PHPT was higher than usual. However mean DBP almost had the usual normal value. It was also noted that the

mean HR had low normal value in both males and females. Mean HR was lower in the male participants than the female participants.

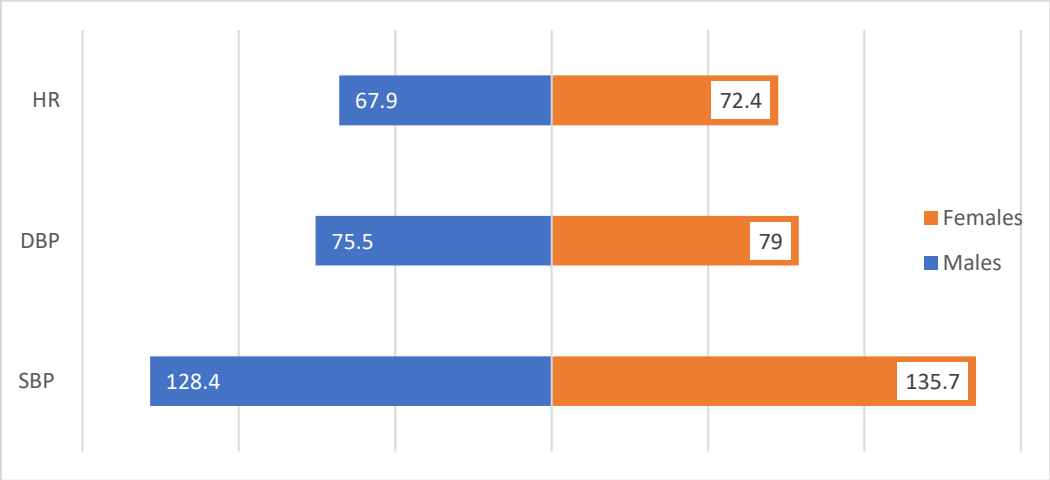


Figure 29- Pictorial representation of general physical examination of study participants

Table 15- Tabular representation of percentage of participants with hypertension and bradycardia

Sign	**Criteria**	**n**	**%**
Systolic hypertension	(SBP>140)	51	39.8
Diastolic hypertension	(DBP>90)	31	24.2
Bradycardia	(HR<60bpm)	14	10.9

In our study it was observed that systolic hypertension was observed in 39.8% (n=51). Diastolic hypertension was observed in 24.2% (n=31). 10.9% (n=14) of the participants had bradycardia.

It was observed that systolic hypertension in the study participants was higher than the usual prevalence. This observation is in line with the previous observation of higher mean SBP.

2.3. b-Local examination (including examination for jaw swelling) and CNS examination (including muscle power)

Table 16-Tabular representation of local and CNS examination of study participants.

Variable	**Male**		**Female**		**Overall**	
	n	Percentage	n	Percentage	n	Percentage
Jaw swelling	4	8.5	4	4.9	8	6.3
Distal Myopathy	11	23.4	44	54.3	55	43.0
Proximal Myopathy	14	29.8	53	65.4	67	52.3

In our study the local and the CNS examination of study participants was done. On local examination palpable jaw swelling was seen amongst 8.5% (n=4) of the males and 4.9% (n=4) of the females.

It was observed that the jaw swelling was more common in the male participants.

In the CNS examination proximal and distal muscle power of the study participants was assessed. Proximal muscle power of less than 5 was seen in 65.4% (n=53) females and 29.8% (n=14) males while the distal muscle power of less than 5 was seen in 54.3% (n=44) of the females and 23.4% (n=11) of the males.

On CNS examination diminished muscle power was more common in the female participants. Diminution of proximal muscle power was more common than distal muscle power.

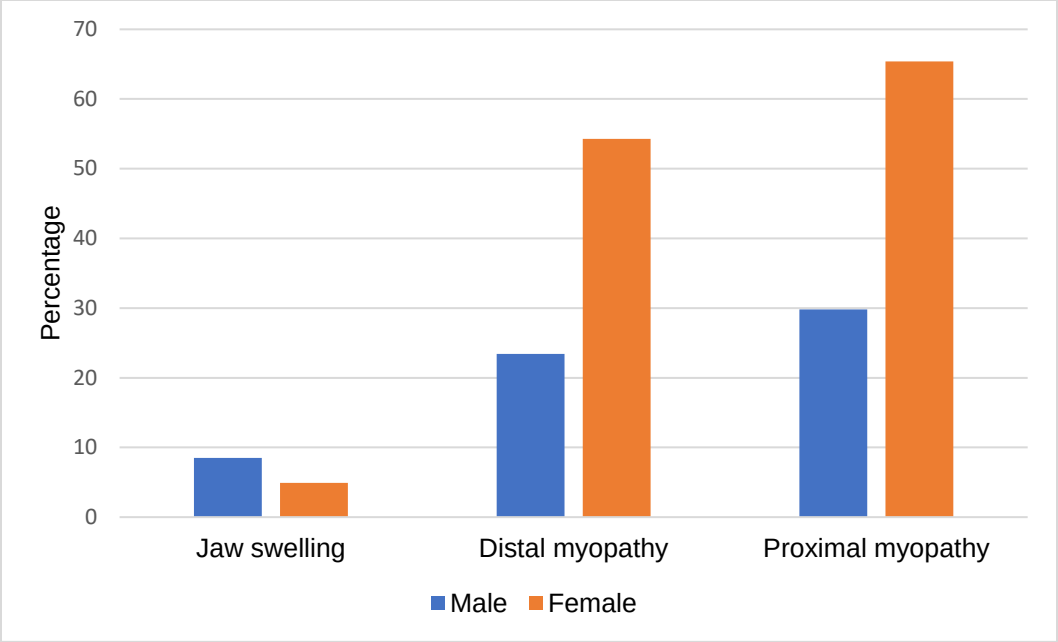


Figure 30 -Pictorial representation of local and CNS examination of study participants.

2.3. c-Mini mental status examination (MMSE)

Table 17-Tabular representation of MMSE of study participants.

MMSE score	**Male**		**Female**		**Overall**	
	n	%	n	%	n	%
Mild impairment (20-24)	9	19.1	17	21.0	26	20.3
Moderate impairment (10-19)	4	8.5	16	19.8	20	15.6
Severe impairment (<10)	0	0.0	0	0.0	0	0.0
Total	**13**	**27.7**	**33**	**40.7**	**46**	**35.9**

In our study Mini Mental Status Examination of the study participants was done. The study subjects MMSE score of less than 24 were 35.9% (n=46) constituting 27.7% (n=13) male participants and 40.7% (n=33) female participants. Mild impairment with MMSE of 20-23 was seen in 20.3% (n=26) constituting 19.1% (n=9) of the male participants and 21% (n=17) of the female participants. Moderate impairment with MMSE of 10-19 was seen in 15.6% (n=20) constituting 8.5% (n=4) of the male participants and 19.8% (n=16) of the female participants. None of the participants had severe impairment with MMSE of less than 10 in both male and female participants.

It was observed that mental impairment was more common in the female participants than the male participants. Patients with mild impairment were more than the patients with moderate impairment.

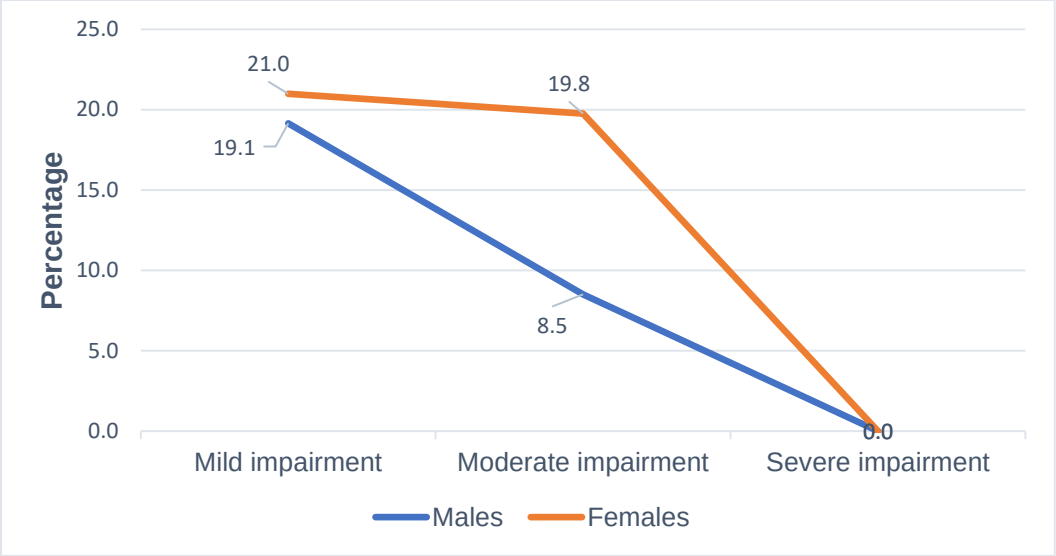


Figure 31-Pictorial representation of MMSE of study participants.

2.3. d-PHQ-4 (Patient Health Questionnaire-4) assessment

Table 18-Tabular representation of PHQ-4 (Patient Health Questionnaire-4) assessment of study participants.

Psychological distress	**Male**		**Female**		**Overall**	
None(0-2)	17	34.0	40	49.4	57	43.8
Mild(3-5)	14	29.8	16	19.8	30	23.4
Moderate(6-8)	7	14.9	5	6.2	12	9.4
Severe(9-12)	9	19.1	20	24.7	29	22.7
Total	**47**	**100**	**81**	**100**	**128**	**100**

In our study psychological distress assessment was done based on the PHQ-4 questionnaire and the distress was graded as none (0-2), mild (3-5), moderate (6-8) and severe (9-12).No psychological distress was seen in 43.8%(n=57) of the study participants constituting 34%(n=17) males and 49.4%(n=40) female participants. Mild distress was seen in 23.4%(n=30) constituting 19.8%(n=16) of the females and 29.8%(n=14) of the males while moderate distress was seen in 9.4% (n=12) constituting 14.9%(n=7) of the males and 6.2%(n=5) of the females. Whereas severe distress was seen in 22.7% (n=29) constituting 19.1% (n=9) of the males and 24.7% (n=20) of the females.

It was observed that psychological distress was more common in the male participants than the female participants. However more female participants had severe psychological distress than the male participants. Almost 1/4th of the females had severe psychological distress.

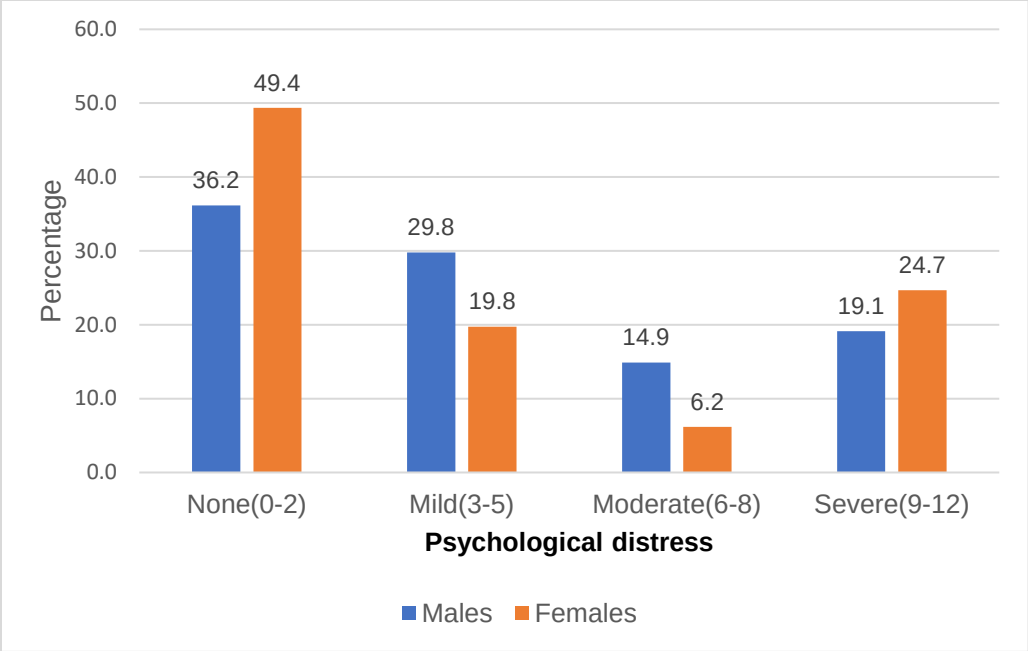


Figure 32- Pictorial representation of PHQ-4 (Patient Health Questionnaire-4) assessment of study participants.

3. Investigational assessment:

3.1 Blood analysis

3.2 Urine analysis

3.3 Cardiological assessment

3.4 Radiological assessment

3.1 Blood Analysis

Table 19- Tabular representation of blood investigation analysis of study participants

Variable	**Male**	**Female**	**p-value**	**Overall**
	Mean ±SD	Mean ±SD		Mean ±SD
Hb(g/dl)	11.5±2.3	9.9±1.9	**<0.001**	10.5±2.2
NLR	4.98±4.9	3.86±2.4	**0.04**	4.2±3.5
Platelets(x103/µl)	273.8±121	219.1±100	**0.003**	239.2±111.5
ALP(U/l)	175±260	209±228	0.22	196.8±243.3
C.Ca(mg/dl)	12.82±1.85	12.03±1.47	**0.005**	12.3±1.6
PTH(pg/ml)	505.6±585.1	546.8±701.2	0.36	531.6±658.8
Vit-D(ng/ml)	22.7±15.6	26.4±25.4	0.18	25.1±23.3
Phosphate(mg/dl)	2.40±0.71	2.37±0.69	0.40	2.3±0.7
Uric acid(mg/dl)	6.2±1.5	5.9±1.1	0.12	6.1±1.3

In our study various blood and biochemical analysis were done in the study subjects. In both the males and the females lower haemoglobin was observed with the mean value of 11.5±2.3 g/dl amongst males and 9.9±1.9 g/dl amongst females. The observed p-value was <0.001 hence there was statistically significant difference in the haemoglobin levels amongst different genders. It was also observed that haemoglobin of <10 g/dl was

seen in 25.5% (n=12) of the male participants and 56.8% (n=46) of the female participants.

NLR was observed to be high with the mean value of 4.98±4.9 amongst the male participants and 3.86±2.4 amongst the female participants. The p-value was observed to be <0.05 hence statistically significant difference was observed with high value amongst the male participants.

In our study the mean platelet levels of 273.8±121 were observed amongst the males while the mean platelet levels of 219.1±100 were observed amongst the females. The p- value observed was 0.003, hence statistically significant difference between the platelet levels and gender was observed. The relative platelet deficiency was observed in the female participants.

Corrected (albumin adjusted) serum calcium levels had mean value of 12.82±1.85 g/dl amongst the male participants and 12.03±1.47g/dl amongst the female participants. The difference observed was statistically significant with p-value of 0.005. It was observed though the number of female participants were more than the male participants, the hypercalcemia observed was more severe amongst the male participants.

In our study PTH had mean value of 505.6±585.1 pg/ml amongst males and 546.8±701.2 pg/ml amongst females with p value 0.22. High PTH level was observed both in males and females but there was no statistically significant difference amongst both the genders. Since PTH levels were following non-normal distribution, median PTH was calculated. The median PTH was 234 (119-690) pg/ml amongst the males and 241 (128-679) pg/ml amongst the females. The overall PTH value had a mean of 531.6±658.8 pg/ml. It was observed that study participants had high PTH levels.

High levels of ALP were observed amongst the study participants with the value of 175±260 U/l in the males and 209±228 U/l in the females. Low

vitamin-D levels were observed with mean of 22.7±15.6 ng/ml in the male participants and 26.4±25.4 ng/ml in the female participants with overall mean of 25.1±23.3 ng/ml. Low levels of phosphate were observed with mean phosphate levels of 2.40±0.71 mg/dl amongst males and 2.37±0.69 mg/dl amongst females with overall mean of 2.3±0.7mg/dl. High levels of uric acid levels were observed with the mean uric acid levels of 6.2±1.5mg/dl in the male participants and 5.9±1.1 mg/dl in the female participants with overall mean of 6.1±1.3 mg/dl.

It was observed that PHPT patients had low Hb, high NLR and low platelet levels. Patients also had high ALP, high corrected serum calcium, high PTH and hyperuricemia. Hypovitaminosis-D and hypophosphatemia were also observed in the study population.

In our study statistically significant lower Hb level and platelet levels were observed in the female participants in comparison to the male participants. Also statistically significant high NLR value was observed in the male participants than the female participants.

Another important observation that was made was statistically significant difference in the mean values of corrected serum calcium levels amongst the males and the females with the p-value of 0.005. It was observed that higher mean calcium was observed in the males. However other biochemical investigations did not have any significant gender difference.

3.2 Urine analysis:

Table 20- Tabular representation of urine analysis of study participants

Variable	**Male**		**Female**	
	n	**Percentage**	**n**	**Percentage**
U.Ca >200mg/24h	37	78.7	59	72.8
U.Ca >400mg/24h	2	4.3	0	0
24h U.Ca (mg/24 hours)	**251.4±61.1**		**233±61.9**	

In our study 24h urinary calcium analysis was done in the study participants. It revealed a mean of 251.4±61.1mg/24 hours amongst the male participants and 233±61.9 mg/24 hours amongst the female participants. Most of the patients had urinary calcium levels between the range of 200-400 mg/24hours. 4.3% (n=2) of the male participants had urinary calcium level of more than 400 mg/24 hours. None of the females had urinary calcium level of more than 400 mg/24 hours.

It was observed that urinary calcium excretion in the males was more than the urinary calcium excretion of the females. Also the observed the serum calcium and the incidence of renal calculi is also higher amongst the male participants.

3.3 Cardiological assessment:

Table 21-Tabular representation of 2D-ECHO findings of study participants.

Assessment of function	Parameter	Criteria	Male		Female		Overall	
			n	%	n	%	n	%
Systolic Dysfunction	EF	<50%	10	32.3	13	23.2	23	26.4
	FS	<27%	9	29.0	14	25.0	23	26.4
Diastolic Dysfunction	E: A	<0.80	11	35.4	29	51.8	51	45.9
Pulmonary Pressures	Normal	≤30	20	64.5	31	55.4	51	58.6
	Mild	31-45	7	22.6	16	28.6	23	26.4
	Moderate	46-60	3	9.6	8	14.2	11	12.6
	Severe	>60	2	6.4	1	1.7	3	3.4
LVH	LVMI	Males≥79	18	58.1				
		Females≥69			29	51.8	47	54
Calcifications	AVC		5	16.1	12	21.4	17	19.5
Total			31	100	56	100	87	100

2D-ECHO was done in 87 study participants. Systolic dysfunction was assessed by EF and FS. EF below the normal range was seen in 32.3% (n=10) amongst the male population and 23.3% (n=13) amongst the female population and FS below the normal range was seen in 29% (n=9)

of the males and in 25% (n=14) of the females. Diastolic dysfunction was assessed on the basis of E: A ratio of less than 0.8. It was seen in 35.4% (n=11) of the males and 51.8% (n=29) of the females.

Pulmonary pressures were assessed by PASP. No pulmonary hypertension was seen in 64.5% (n=20) of the male participants and 55.4% (n=31) of the female participants. Mild PH was seen in 26.4% (n=23) of the study participants constituting 22.6% (n=7) of the male participants and 28.6% (n=16) of the female participants. Moderate PAH was seen in 12.6% (n=11) of the study participants constituting 9.6% (n=3) of the males and 14.2% (n=8) of the females. Severe PAH was seen in 3.4% (n=3) of the study participants constituting 6.4% (n=2) amongst the males and 1.7% (n=1) amongst the females.

For assessment of LVH, LVMI was calculated on the basis of recorded LVID, IVS and PW assessed on echography. LVH was seen in 58.1% (n=18) amongst the males and 51.8% (n=29) amongst the females. AVC was seen in 16.1% (n=5) amongst the males and 21.4% (n=12) amongst the females.

It was observed that in cardiac assessment the male participants were observed to have more systolic dysfunction, PAH and LVH while the female participants showed more diastolic dysfunction and AVC.

In our study it was observed that the PHPT patients had cardiac involvement more than usual. However such high prevalence of cardiac abnormalities can also be attributed to high prevalence of prior comorbidities. DM, HTN, CAD and CVA are known to be the independent risk factors for cardiac morbidity and mortality. Hence PHPT may not be the sole contributor for cardiac involvement in our study.

3.4 Radiological analysis:

Table 22– Tabular representation of various radiological assessment done in study subjects.

Investigations	Male			Female			Overall		
	N	+	%	N	+	%	N	+	%
USG neck (N=121)	43	37	86.0	78	64	82.0	121	101	83.4
Tc-99(N=117)	43	38	88.4	74	66	89.1	117	104	88.9
X-ray(N=94)	37	12	32.4	57	18	31.5	94	30	31.9

In our study patients were subjected to various radiological investigations and analysis was noted. USG- neck was done in 121 study participants. 83.4% (n=102) of study participants showed sonological evidence of parathyroid adenoma constituting 86% (n=38) of the male participants and 82% (n=64) of the female participants. Tc-99 sestamibi spect scan was done in 117 study participants. 88.9% (n=104) showed the evidence of parathyroid adenoma constituting 88.4% (n=38) of the male participants and 89.1% (n=66) of the female participants. X-Ray bilateral hands and wrist, skull or spine was done in 94 study participants. Only 31.9% (n=94) showed radiological evidence of bony involvement constituting 32.4% (n=12) of the male participants and 31.5% (n=18) of the female participants.

It was observed that USG-neck showed more evidence of parathyroid adenoma in the male participants as compared to the female participants. Rest of the radiological assessment did not show any gender variation

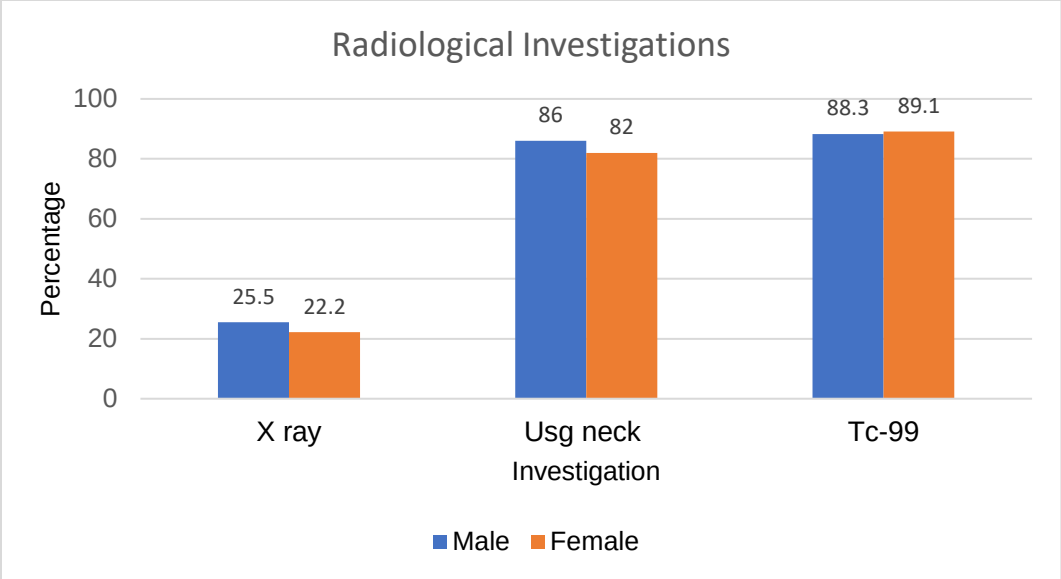


Figure 33– Pictorial representation of various radiological assessment done in study subjects.

In our study 11 patients did not undergo Tc-99 sestamibi spect scan. Out of these 11 patients PET-CT was done in one patient which was suggestive of RIPA and CT-neck was done in 3 patients which localised adenoma. Out of 13 Tc-99 negative patients, they were subjected to CT-neck which showed RIPA in 1 patient while CT-neck was non-significant in 1 participant. 1 patient underwent MRI-neck and 1 patient underwent PET-CT, both were suggestive of RIPA. Out of 13 Tc-99 negative patients, 11 patients had ultrasonographic evidence while 2 patient did not show any USG lesion as well.

3.4. b- Sensitivity and specificity

In our study histopathological examination was considered as gold standard. The sensitivity and specificity of tests (Tc-99 and USG- Neck) were analysed after formation of 2x2 table.

Table 23- 2x2 tabulation comparing Histopathology analysis (GS) and Tc-99 sestamibi spect scan (Test) for sensitivity and specificity assessment

		Biopsy		Total
		+	-	
Tc-99	+	64	2	66
	-	2	4	6
Total		66	6	

Sensitivity =TP/ (TP+FN) =96.9%

Specificity= TN/ (TN+FP) =66.7%

Table 24- 2x2 tabulation comparing Histopathology analysis (GS) and USG- Neck (Test) for sensitivity and specificity assessment

		Biopsy		Total
		+	-	
USG-Neck	+	56	4	60
	-	11	2	13
Total		67	6	

Sensitivity =TP/ (TP+FN) =83.5%

Specificity= TN/ (TN+FP) =33.3%

3.4. c- Pre-surgery localization

Table 25- Tabular presentation of pre-surgery localisation of parathyroid adenoma in study subjects

Localization	Male		Female		Overall	
	n	%	n	%	n	%
LIPA	17	44.7	29	43.9	46	44.2
RIPA	16	42.1	29	43.9	45	43.3
LSPA	2	5.3	1	1.5	3	2.9
RSPA	1	2.6	3	4.5	4	3.8
Ectopic	2	5.3	4	6.1	6	5.8
Total	38	100	66	100	104	100

In our study localisation of parathyroid adenoma was done on the basis of Tc-99 sestamibi spect scan. Localisation from most to least common was LIPA (44.2%), RIPA (43.3%), ectopic (5.8%), RSPA (3.8%) and LSPA (2.9%).

It was observed that inferior parathyroid adenoma was more common than superior parathyroid adenoma. In our study ectopic parathyroid adenoma tissue was more common than the superior parathyroid adenoma. Most common site for localisation of ectopic parathyroid adenoma was mediastinum. In mediastinum lesion was mostly localised to anterior mediastinum.

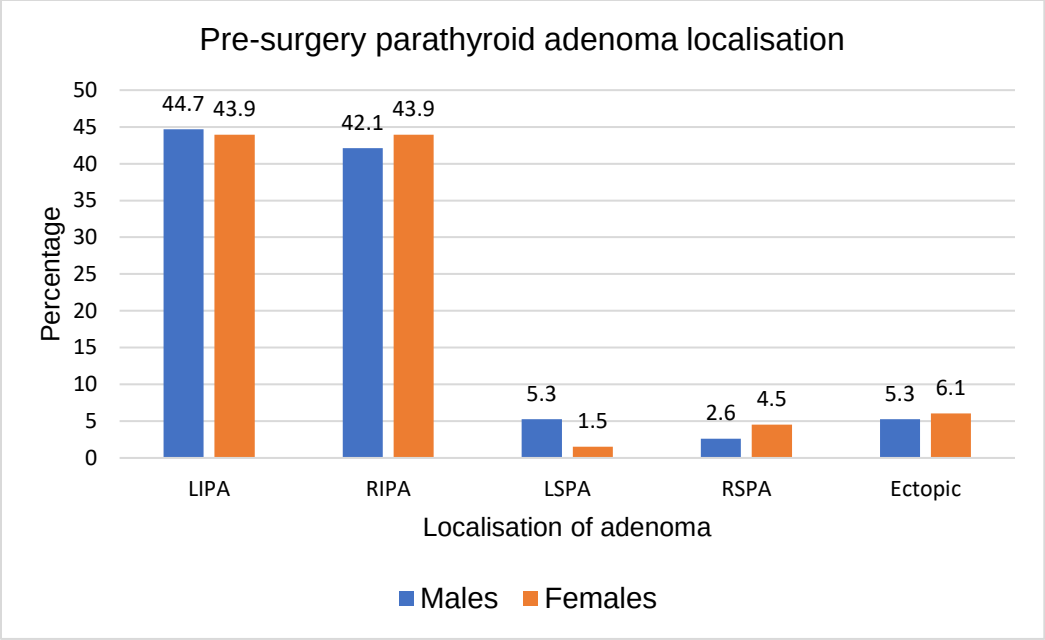


Figure 34-Pictorial presentation of pre-surgery localisation of parathyroid adenoma in study subjects

3.4. d -USG W/A

Table 26-Tabular representation of various USG-W/A findings in study participants

USG-W/A	**Male**		**Female**		**Overall**	
	n	%	n	%	n	%
Acute pancreatitis	11	30.6	10	15.2	21	20.6
Chronic pancreatitis	1	2.8	5	7.6	6	5.9
Renal Calculi	8	22.2	13	19.7	21	20.6
Renal parenchymal changes	2	5.6	8	12.1	10	9.8
Not significant	14	38.9	30	45.5	44	43.1
Total	**36**	**100**	**66**	**100**	**102**	**100**

In our study USG-W/A was done in 102 patients. Acute pancreatitis was revealed in 20.6% (n=21) of the study participants constituting 30% (n=11) of the male participants and 15.2% (n=10) of the female participants. Chronic pancreatitis was revealed in 5.9% (n=6) of the study participants constituting 2.8% (n=1) of the male participants and 7.6% (n=5) of the female participants. Renal calculi was revealed in 20.6% (n=21) of the study participants constituting 22.2% (n=8) of the males and 19.7% (n=13) of the females. Renal parenchymal changes were seen in 9.8% (n=10) of the study participants constituting 5.6% (n=2) of the male participants and 12.1% (n=8) of the female participants. In the rest of the participants USG-W/A findings were insignificant.

It was observed that acute pancreatitis and renal calculi were more common amongst the male participants while chronic pancreatitis and renal parenchymal changes were more common amongst the female participants.

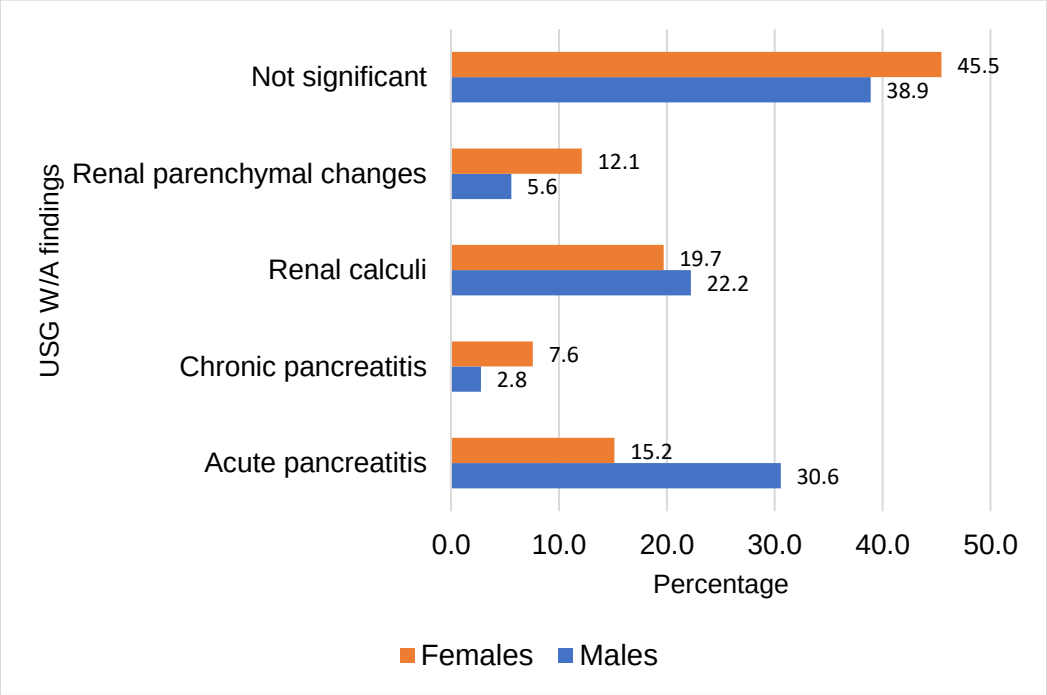


Figure 35- Pictorial representation of various USG-W/A findings in study participants

4. Treatment:

Table 27- Tabular representation of patients presented to OPD compared with patients presented to IPD

Patient	Male		Female		Overall	
	n	**%**	**n**	**%**	**n**	**%**
OPD	10	21.3	24	29.6	34	26.6
IPD	37	78.7	57	70.4	94	73.4
Total	**47**	**100**	**81**	**100**	**128**	**100**

In our study the study participants presenting to both OPD and admitted in IPD were noted. Of the study participants 26.6% (n=34) presented to OPD constituting 21.3% (n=10) of the male participants and 29.6% (n=34) of the male participants. 73.4% of the study participants were admitted constituting 78.7% (n=37) of the male participants and 70.4% (n=57) of the female participants.

It was observed that more number of the female participants were treated on OPD basis and more number of the male participants were admitted and treated in IPD.

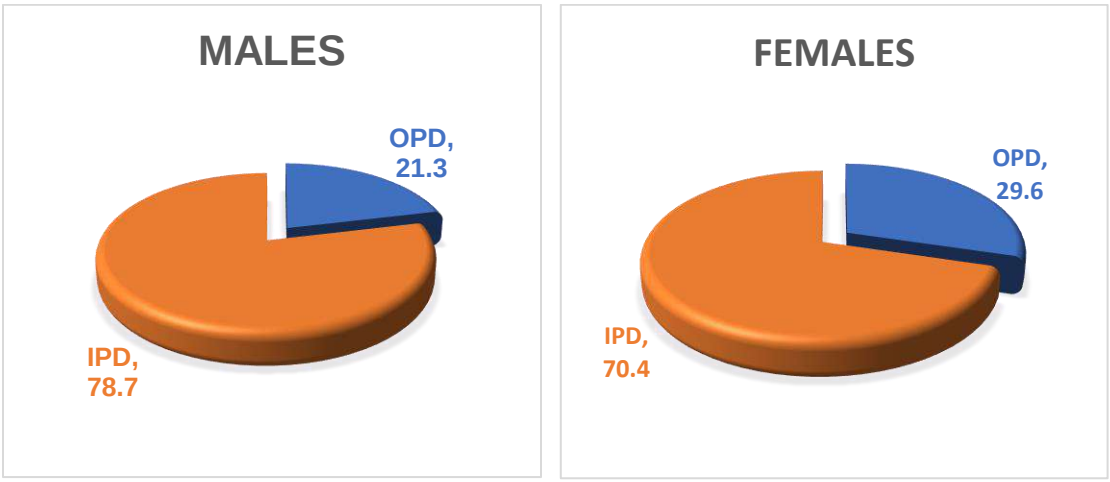


Figure 36-Pictorial representation of patients presenting to OPD compared to IPD in the males and the female participants

4. b- Treatment offered

Table 28-Tabular representation of various treatment options offered to the study participants.

Treatment	Males			Females			Overall		
	n	% (N=37)	Total % (N=47)	n	% (N=57)	Total % (N=81)	n	% (N=94)	Total % (N=128)
IVF	31	83.8	66	52	91.2	64.2	83	88.3	64.8
Furosemide	32	86.5	68.1	51	89.5	63.0	83	88.3	64.8
Calcitonin	30	81.1	63.8	51	89.5	63.0	81	86.2	63.3
Cinacalcet	26	70.3	55.3	45	78.9	55.6	71	75.5	55.5
Zoledronate	12	32.4	25.5	32	56.1	39.5	44	46.8	34.4
Denosumab	5	13.5	10.6	7	12.3	8.6	12	12.8	9.4
HD	1	2.7	2.1	4	7.0	4.9	5	5.3	3.9

In our study treatment offered to the IPD patients was noted. Most to least common treatment modality used in the admitted patients included IVF hydration (88.3%), diuretics (88.3%), calcitonin (86.2%), cinacalcet (75.5%), zoledronate (46.8%), denosumab (12.8%) and hemodialysis (5.3%). Gender distribution of treatment modalities was tabulated.

Four patients were received in fluid overload with reduced EF, in them only the loop diuretics were used without IVF. Four patients were received in grossly dehydrated state, in them only IVF hydration was used without furosemide.

Zoledronate was used in 32.4% (n=12) of the male participants and 56.1% (n=32) of the female participants. Denosumab was used in 13.5% (n=5) of the male participants and 12.3% (n=7) of the female participants.

It was observed that most common modality was saline hydration with forced diuresis. Persistent and non-responding hypercalcemia was more commonly observed in the female participants requiring use of zoledronate and denosumab. Use of zoledronate was more common in the female participants and the use of denosumab was more common in male participants.

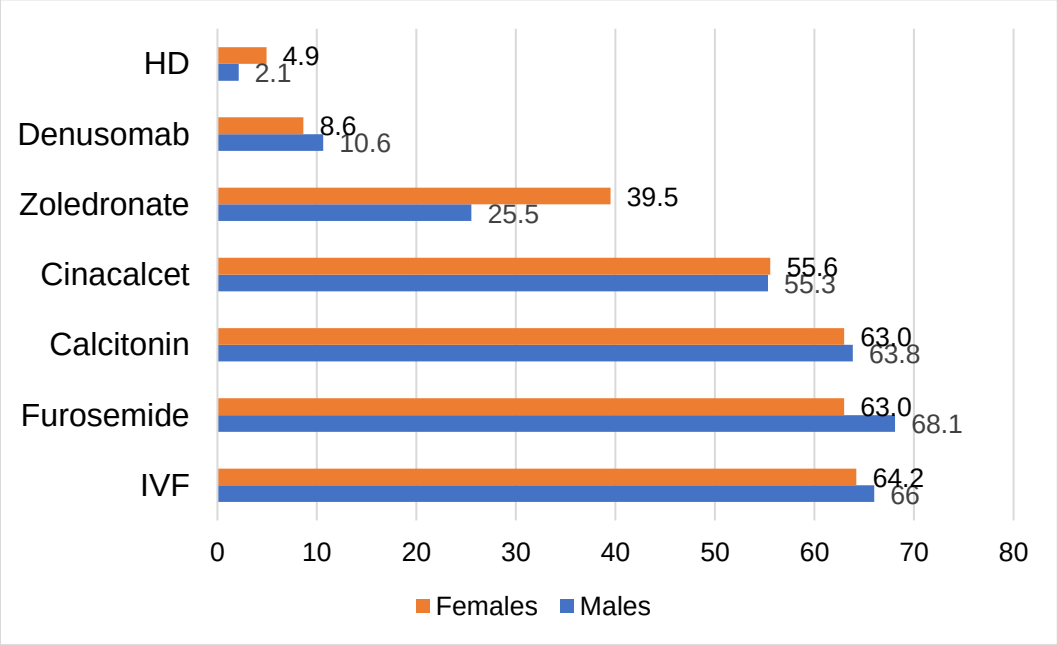


Figure 37- Pictorial representation of various treatment options offered to different study participants.

Table 29- Tabular representation of mean number of days to the normalisation of calcium post treatment

	Male		Female		Overall	
No. of days:	**Mean(D)**	**SD**	**Mean(D)**	**SD**	**Mean(D)**	**SD**
Hospitalization	8.4	3.5	9.1	3.9	8.9	3.7
Zoledronate	4.3	1.4	3.4	1.2	3.6	1.3
Denosumab	3.5	0.5	4.1	1	3.9	0.9

In our study after the start of the treatment the number of days to the normalisation of calcium were noted. Mean number of days to normalisation of calcium after hospitalisation were 8.9±3.7 days. Mean number of days to normalisation of calcium after zoledronate were 3.6±1.3 days. Mean number of days to normalisation of calcium after denosumab were 3.9±0.9 days.

It was observed that the mean number of days to normalisation of calcium after hospitalisation in the female participants were more than the mean number of days to normalisation of calcium after hospitalisation of the male participants.

In our study it was observed that more number of the female participants had persistent and non-responding hypercalcemia requiring zoledronate and denosumab. Also the duration to normalisation of calcium in the female participants was more than the male participants.

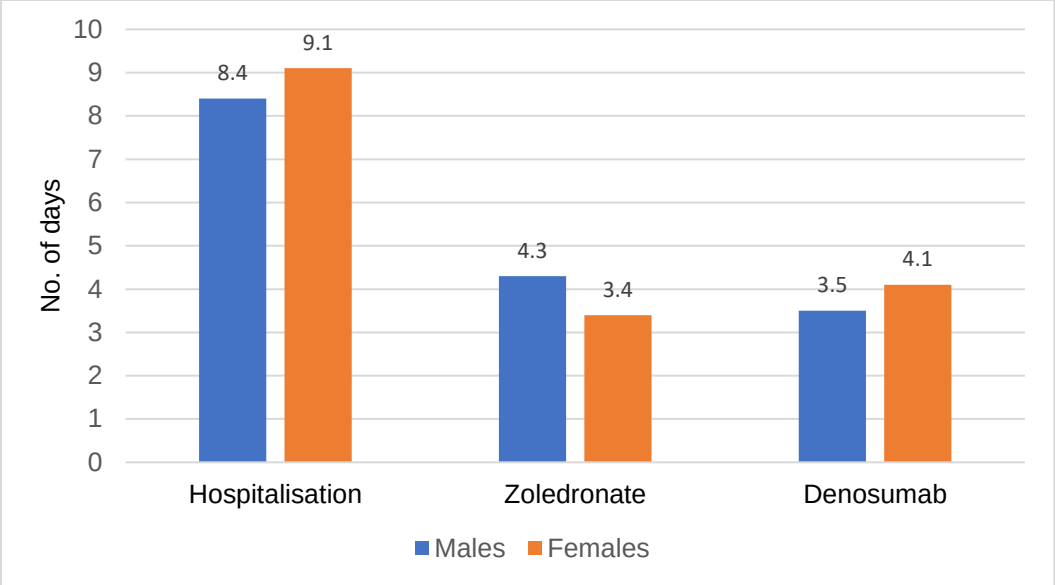


Figure 38- Pictorial representation of mean number of days to normalisation of calcium post treatment.

4. c- Post parathyroidectomy:

Table 30- Tabular representation of percentage of study participants operated and post-op analysis

	Male			Female			Overall		
	n	**% (N=37)**	**Total% (N=47)**	**n**	**% (N=57)**	**Total% (N=81)**	**n**	**% (N=94)**	**Total% (N=128)**
Operated	33	89.2	70.2	44	77.1	54.3	77	81.9	60.2
HBS	4	10.8	8.5	6	10.5	7.4	10	10.6	7.8
Mean size (cm)	2.4x1.5x0.7			2.4x1.4x0.8			2.4x1.5x0.7		
Mean weight (g)	6.9±5			7.2±5.6			7.1±5.3		

In our study surgical details of the study subjects were noted. Amongst the admitted male participants 89.2% (n=33) got operated and 10.8% (n=6) of the operated patients had HBS. The mean size of excised adenoma was 2.4x1.5x0.7cm. The mean weight of excised adenoma was 6.9±5g. On the other hand 77.1% (n=44) amongst the admitted female participants were operated and 10.5% (n=6) of the operated participants had HBS. The mean size of excised adenoma was 2.4x1.4x0.8cm. The mean weight of excised adenoma was 7.2±5.6g.

It was observed that number of the female participants operated were quite less than the male participants operated. HBS was overall observed in 10.6% of the participants. No gross gender difference was seen for mean size and mean weight of excised adenoma.

Table 31- Tabular representation of histopathological analysis of the specimen of study participants.

Histology									
	Male			Female			Overall		
	n	% (N=33)	Total% (N=47)	n	% (N=44)	Total% (N=81)	n	% (N=77)	Total% (N=128)
PA	29	87.8	61.7	36	81.8	44.4	65	84.4	50.8
PCA	2	6.1	4.3	4	9.1	4.9	6	7.8	4.7
INC	2	6.1	4.3	4	9.1	4.9	6	7.8	4.7

Amongst the male participants 87.8% (n=29) had parathyroid adenoma and 6.1% (n=2) had parathyroid carcinoma while histopathological analysis was inconclusive in 6.1% (n=2). While amongst the female participants 81.8% (n=36) had parathyroid adenoma and 9.1% (n=4) had parathyroid carcinoma while histopathological analysis was inconclusive in 9.1% (n=4). It was observed that histologically parathyroid adenoma was much more common than the parathyroid carcinoma.

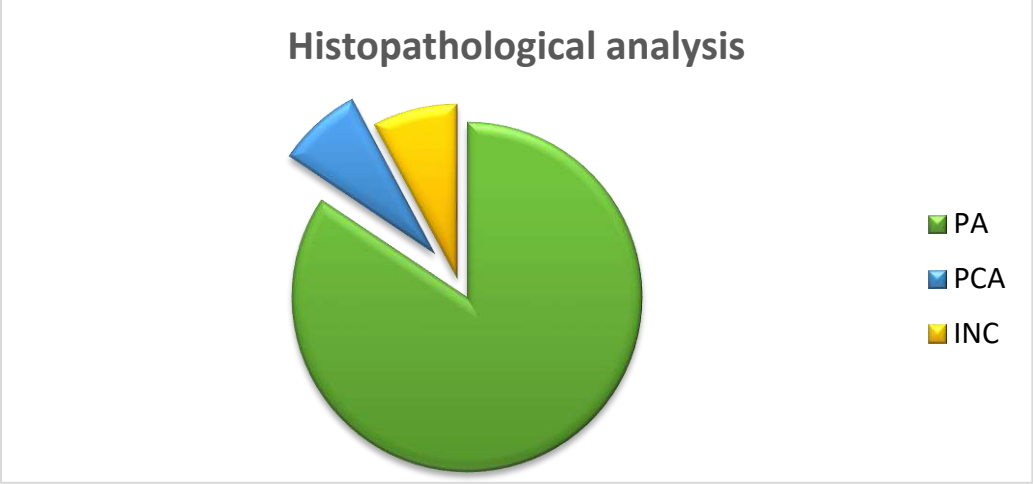


Figure 39- Pictorial representation of histopathological analysis of the specimen of study participants.

5. Follow-up:

Table 32 -Tabular representation of outcome of follow-up of study subjects

	Male		**Female**		**Overall**	
	n	**%**	**n**	**%**	**n**	**%**
Followed	44	93.6	74	91.3	118	92.2
LTFU (lost to follow-up)	3	6.4	4	4.9	7	5.5
EXP	0	0	3	3.7	3	2.3

In our study the outcome of the patients was noted. It was noted that 92.2% (n=118) of the study subjects were followed, 5.5% (n=7) of the study subjects were lost to follow up and 2.3% (n=3) expired. Out of three patients who succumbed to the illness one patient expired due to post-op hypocalcaemia while others expired due to arrhythmias due to hypercalcemia.

Table 33- Tabular representation of mean corrected serum calcium and serum PTH within 1-6 months duration

Follow-up	Male		Female		Overall	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
S.Ca	9.04	0.77	9.07	0.93	9.05	0.86
S.PTH	21.59	37.26	37.19	107.9	31.03	87.4

In our study on follow up the mean serum calcium and mean serum PTH of study participants were calculated. Amongst the male participants the mean serum calcium level was 9.04±0.77 mg/dl with the mean PTH level of 21.59 ± 37.26 pg/dl. The number of patients with persistent hypercalcemia amongst the male participants were 13.6% (n=6). The serum albumin levels were not assessed for every patient on follow-up, the average serum albumin at initial presentation was 3.7 so to make the data comparable the correction factor was used accordingly.

While amongst the female participants the mean serum calcium level was 9.07±0.93 mg/dl with mean PTH level of 37.19±107.9 pg/dl. Number of patients with persistent hypercalcemia amongst the female participants were 5.4% (n=4).

DISCUSSION

Primary hyperparathyroidism is a common endocrinal disorder with varied clinical and biochemical findings with different medical and surgical treatment modalities available. Our current study aimed to study the clinical profile of patients presenting with primary hyperparathyroidism in a tertiary care hospital. A prospective cross-sectional study was conducted from 15th September 2022 to 31st December 2023 with a total enrollment of 128 patients. Data obtained was compared with previously published literature to obtain the discussion. Cases were followed up once between 1-6 months with follow-up serum calcium and serum PTH.

1. Demographic data-

In our study of 128 enrolled participants 36.7% (n=47) were males and 63.3% (n=81) were females. Hence females were accounting for 2/3rd of the study participants. The ratio of male to female was 1:1.7 which indicated that the females were more commonly affected than the males. Similar results were observed in the studies conducted elsewhere. Thanveer *et al.*[98](M: F ; 1:1.7), Maskey *et al.* [99](M: F;1:2.1), Pardeep *et al.*[36] (M: F ; 1:2.3), Arora et al[9] (M: F ;1:2.3) and Bhansali *et al.* [64](M: F ;1:3.3) also found female preponderance of patients with primary hyperparathyroidism. This concludes that female gender was a significant risk factor for PHPT in our study which was in line with other studies.

In our study the mean age of patients at the time of diagnosis was 53.3±14.2 years. The age range of patients was 19-82 years. It was observed that the maximum number of patients were observed in the age group of more than 50 years. Mean age at diagnosis has been reported by various other studies also. The mean age at diagnosis was slightly higher in our study. Bhansali *et al.* [64] (36.3 years), Thanveer *et al.* [98] (47 years) and Maskey *et al.* [99] (43 years) also showed predominance in elderly age groups. It can be concluded that PHPT is a disease

predominantly diagnosed in elderly population. Hence PHPT is a disease with elderly female preponderance.

In our study the mean duration of the symptoms prior to the diagnosis was 24.03±17.7 months. The range of duration of illness prior to diagnosis was 0-78 months. It was seen that approximately 1/3rd of the study population presented within the first year of symptom onset and more than ½ of the study participants were diagnosed within 2 years of the symptom onset. Pardeep *et al.* [36] in 2011 reported mean duration of illness prior to diagnosis as 84 months. Jha *et al.* [100] in 2016 reported that the mean duration of symptoms prior to diagnosis was shorter in the recent group (Group B-2007 to 2015) i.e. 26 months as compared to older group (Group A-1994 to 2007) i.e. 38 months. The progressive shorter duration prior to diagnosis can be attributed to early detection and diagnosis confirmation due to increased awareness and routine testing in the modern times.

Relative to the males, females had delayed peak in diagnosis from 25-36 months of symptom onset which can be attributed to lower median serum calcium in female participants. Lower median serum calcium corresponds to decreased severity of symptoms and hence delayed presentation to hospital. Another reason which can be attributed includes shear male dominance in Indian society leading to decreased medical facilities availability to female population. Moreover severe acute hypercalcemia induced symptoms were more commonly seen in the males which warrant early medical care.

2. Clinical presentation and examination-

In the era between 1930 and 1970 PHPT was considered as a symptomatic disease with overt skeletal or renal complications. However in the modern times the severity of symptoms have decreased with a relative shift towards asymptomatic presentation. In our study the most common overall clinical presentation was bony involvement (44.1%)

followed by gastrointestinal (43.4%), neuropsychiatric (40.6%), renal (31.3%) and asymptomatic (16.4%).

In our study gastrointestinal, renal and neuropsychiatric symptoms were more common in the males while females usually presented with bony involvement, chronic pancreatitis or even asymptomatic presentation.

Hence in our study it was observed that males had acute severe clinical presentations while the females had subacute to chronic duration mild-moderate manifestations. The increased severity of symptoms probably attributed to relatively early diagnosis and decreased duration of symptoms prior to diagnosis.

Another observation which can be associated was that there was statistically significant difference in the mean serum calcium levels amongst the males and the females. Hence severe hypercalcemia induced acute symptoms like acute pancreatitis, renal calculi or neuropsychiatric disturbance were more common in the male participants. In line with our study, the study conducted by Arora et al [9] highlighted that patients with acute pancreatitis as index presentation of PHPT were more commonly males. PHPT patients with pancreatitis also had higher serum calcium levels than the PHPT patients without pancreatitis.

The manifestations involving chronic mild-moderate hypercalcemia were more commonly observed in the female participants like bony involvement in the form of chronic bony pains. More prevalence of recurrent bony fractures in the females can also be attributed to concomitant age related osteoporosis.

Table 34– The tabular representation of clinical manifestations in the different studies conducted in the esteemed centres of India in last 20 years

	Renal stones	**Bony pains**	**Fractures**	**Pain abdomen**	**Neuro-psychiatric**	**Asympt**
Current study (2024)	22.7	72.7	15.6	53.9	40.6	16.4
Bhansali *et al.* (2004) [64]	19	67	48	39	23.1	-
Pardeep *et al.* (2011) [36]	21	67	48	-	23	-
Maskey *et al.* (2013) [99]	49	77	40	-	26.4	5.6
Jha *et al.* (2016) [100]	11.8	72	0	-	-	-
Arora *et al.* (2021) [9]	26.7	53.3	23.3	23.3	30	-
Thanveer *et al.* (2023) [98]	34.2	47.4	7.9	44.7	5.3	2.63

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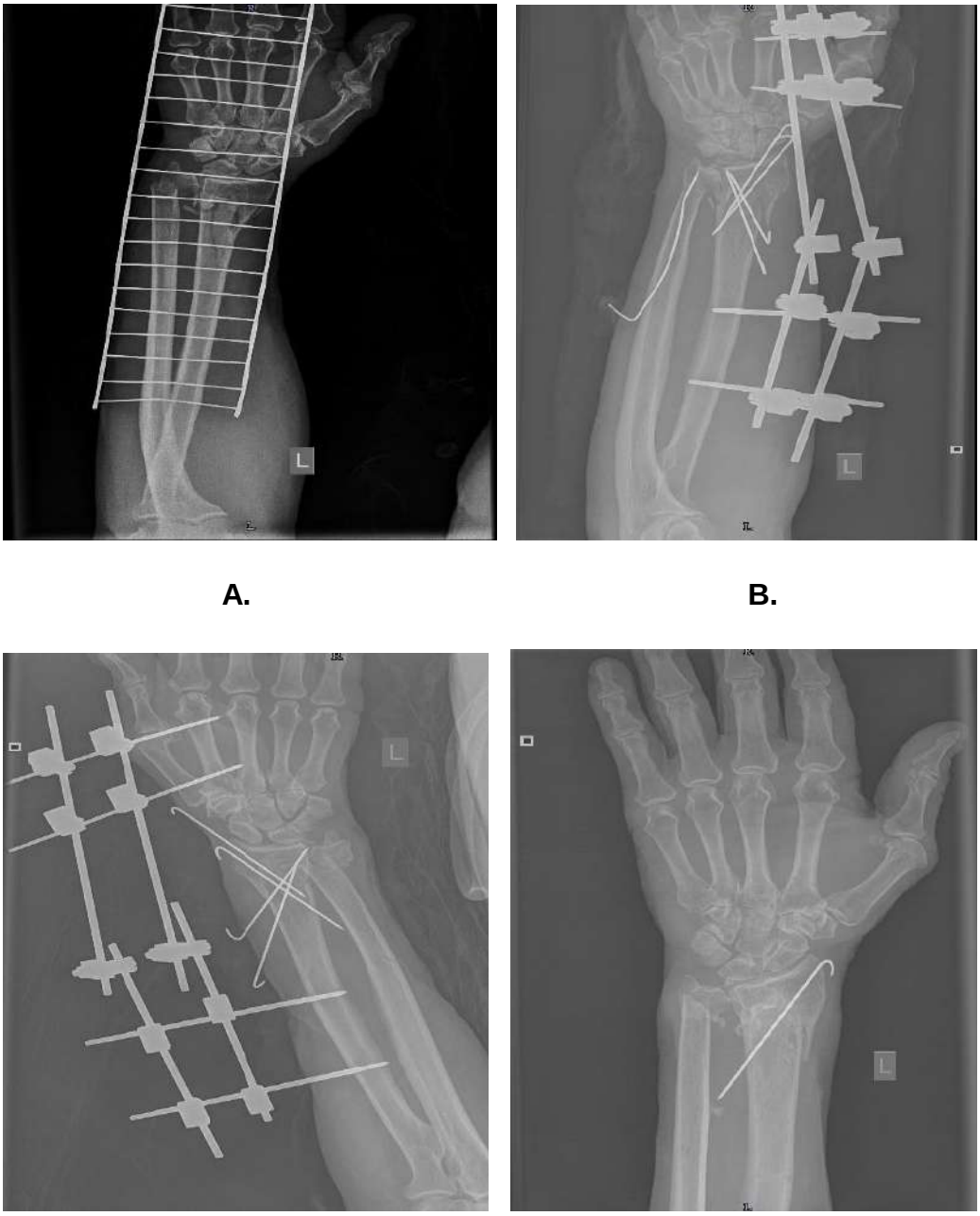
In our study in the renal involvement, polyuria (48.4%) was the most common followed by hematuria and renal stones. In the study by Bhansali *et al.* [64] renal manifestation were seen in the form of polyuria (37 %), graveluria (19%) and hematuria (6%). The systematic meta-analysis conducted by Pardeep *et al.* [36] revealed renal disease in 36% with presence of renal calculi in 21% of the participants. In our study renal

calculi was seen in 22.7% of the study participants. Similar prevalence was also seen in a study conducted by Arora S.et al [9] (26.7%) and Thanveer *et al.* [98] (34.2%).

In our study bony pains were seen in 72.7% of the participants. Similar high prevalence was also seen in various studies including Maskey *et al.* [99] (77%), Pardeep *et al.* [36] (67%), Arora *et al.* [9] (53.3%) and Thanveer *et al.* [98] (47.4%). Jha *et al.* [100] reported bony pains in 72% in recent group but lower incidence in older group (39.3%). Hence it was concluded that bony pains were the most common PHPT presentation with increasing prevalence in the modern times. Increased awareness of symptoms of PHPT over the period of time, routine calcium analysis and early diagnosis has probably contributed to the decreased presentation as severe life threatening symptoms and hence increased prevalence of mild symptoms like bony pains as presenting symptom.

In our study the prevalence of bony fractures was 15.6%. Temporal decline in relative prevalence of bony fractures was documented. Decreasing prevalence of bony fractures was seen in the studies conducted by Bhansali *et al.* [64] (2004) (48%), Pardeep *et al.* [36] (2011) (48%), Maskey *et al.* [99] (2013) (40%), Arora *et al.* [9] (23.3%) and Thanveer *et al.* [98] (2023) (7.9%). Hence over the years the relative decline in the prevalence of severe manifestation in the form of bony fractures was probably due to increased awareness of symptoms of PHPT over the period of time, routine calcium analysis leading to the early diagnosis of the disease. It has led to diagnosis of PHPT in relatively benign phase or even asymptomatic phase.

In our study a 71 year old male patient (Patient-9) presented to hospital and was admitted in department of orthopedics with recurrent fractures at multiple sites. The etiology of multiple fractures was later diagnosed as primary hyperparathyroidism.



A. **B.**

C. **D.**

Figure 40- Pictorial representation of fracture stabilisation of distal end of radius and distal end of ulna (Patient-9).Temporal pattern shown A. 20/9/23 B. 23/9/23 C. 14/10/23 D. 17/12/23

Such cases warrant lower physician suspicion of PHPT for early diagnosis to decrease the long term morbidity of the patients by timely intervention**.**

In our study in the gastrointestinal symptoms, pain abdomen was most common presentation amongst the male participants and constipation was the most common presentation amongst the female participants. Though the similar percentage of patients presented with constipation (57.4% males and 54.3% females) there was difference in the percentage of patients presenting with pain abdomen (61.7% males and 49.4% females).The probable reason which was attributed to the difference in the percentage of pain abdomen in the males and the females is the relatively high incidence of pancreatitis in PHPT which has male preponderance and presentation as acute abdomen. This observation is seen in line with the study by Arora et al [9] in which acute pancreatitis in patients with PHPT was studied and it was concluded that the PHPT patients with pancreatitis had male predominance with relative young age at onset.

In our study prevalence of pancreatitis was 21.1%. Similar prevalence was reported in the studies by Maskey *et al.* [99] (27%) and Bhansali *et al.* [64] (21%).However the lower prevalence was reported by Jha *et al.*[100] (6.7%) and Gopal *et al.*[101] (3%).This difference on critical analysis was attributed to different geographical location leading to different environmental exposure (including air, soil, water) and genetic makeup of individuals. Our current study, Maskey *et al.*[99] and Bhansali *et al.*[64] were done in North India and Jha *et al.* [100] and Gopal *et al.* [101] were done in South India. Hence it was concluded that PHPT presenting as pancreatitis was more common in north India. In our study it was observed that pancreatitis was more common in the male participants and overall the mean age of male participants was lower than the female participants. Hence PHPT induced pancreatitis was more common in younger North Indian males.

Figure 41- Pictorial representation of CT imaging of a young male presented with acute pancreatitis: etiology- PHPT (Patient-42)

In our study the neuropsychiatric manifestations were seen in 40.6% of the participants. In the various studies it was observed that prevalence of neuropsychiatric manifestation ranged mostly from 20-40%. The prevalence of neuropsychiatric manifestations in the study by Bhansali *et al.* [64] was 23.1%, in Pardeep *et al.* [36] was 23%, in Maskey *et al.* [99] was 26.4% and Arora *et al.* [9] was 30%. However the lower prevalence of neuropsychiatric manifestations was seen in Thanveer *et al.* [98] (5.3%) and Gopal *et al.* [101] (2%).

In our study the patients presenting in asymptomatic phase were 16.4% of the study participants. Data about asymptomatic presentation has been observed in very less number of studies. A study by Maskey *et al.*[99] observed asymptomatic presentation in 5.6% of the participants and Thanveer *et al.*[98] observed asymptomatic presentation in 2.63%. However the western population [102] observed asymptomatic as the most common presentation of PHPT in >80% of the study participants. There was a gradual temporal increase in asymptomatic presentation as primary presentation of PHPT being witnessed even in the developing countries. Such an observation was attributed to increased awareness and routine serum calcium analysis leading to early diagnosis in symptom free stage.

In our study higher prevalence of prior comorbidities like DM (50%), HTN (50%), CVA (16.4%) and CAD (14.1%) was observed. In line with our study prevalence of hypertension observed in Bhansali *et al.* [64] was 42%. Even the studies conducted in the developed countries have similar observations. In a study by Fischer *et al.* [103] high prevalence of concomitant HTN (40-60%), diabetes (8-15.9%) and CAD (6.95%) was observed. Higher than usual presentation of comorbidities was attributed to the reason of PHPT being a chronic inflammatory disease. Taylor *et al.* [66] in a study observed high insulin resistance in patients with PHPT which was attributed to high intracellular calcium levels.

In our study systolic hypertension (mean SBP 133 mm Hg) and low normal heart rate (mean 77.7 bpm) was observed. In our study systolic hypertension was seen in 39.8% of the study participants. Our observation was in line with Bhansali *et al.* [64] (mean SBP=133 mm Hg) and Fischer *et al.* [103] (mean SBP=127.2 mm Hg). However mean diastolic BP had usual value (mean DBP <80 mmHg) in our study which was also in line with other studies [103].

In our study jaw swelling was observed in 6.3% participants constituting more commonly the male participants (8.5%) than the female participants (4.9%).The prevalence of jaw swelling observed ranges from 4%-39%.Various studies have observed jaw swelling including Maskey *et al.* [99] (4%), Gopal *et al.* [101] (22%)and Pardeep *et al.* [36] (39%).

In our study it was observed that diminution of proximal muscle power (52.3%) was more common than distal muscle power (43%). It was also observed that diminution of muscle power amongst the female participants (65.4%) was more common than the male participants (29.8%). These findings were in line with observation by Pardeep *et al.* [36] where proximal myopathy was seen in 54.1% of the participants. Similar findings were also observed in developed population by Fischer *et al.* (103) where myopathy was observed in 56% of the study participants. The hypothesis leading to

skeletal muscle weakness was attributed to hypercalcemia induced raised threshold leading to inhibition of depolarisation of nerve and muscle fibres.[104]

In our study cognitive decline with MMSE <24 was observed in 35.9% of the study participants constituting more commonly the female participants (40.7%) than the male participants (27.7%).This observation was attributed to the finding that PTH2 receptors are scattered in the cerebral cortex especially limbic, hypothalamic periventricular neurons and median eminence. Hence cognitive decline is speculated to be associated with the PTH levels in PHPT. [105]

In our study psychological distress assessed by PHQ-4 questionnaire was more common in the male participants (63.8%) than the female participants (50.7%). However ¼ of the female participants had severe distress. The research on psychological assessment amongst PHPT is hotspot with limited data available till date. The recent systematic review on MDD in PHPT was done by Desai *et al.* [106] in 2023 concluded that a major correlation exists between PHPT patients with high serum Ca levels, high serum PTH levels, high serum ALP levels and the depressive symptoms. Moreover various studies had also highlighted the reversibility of neurocognitive decline and psychological distress after surgical intervention.[105,106]

3. Investigational assessment:

In our study it was observed that mean Hb was 10.5 g/dl with mean Hb of 11.5 g/dl in the male participants and 9.9 g/dl in the female participants which is consistent with mild-moderate anaemia in study participants. Statistically significant difference (p-value= <0.001) in the Hb of the males and females was observed. Hb in females was less as a usual observation seen in general population because of regular menstrual loss and less nutritional intake by Indian females. Neutrophil to lymphocytic ratio of the

study participants was calculated as 4.2 with 4.98 in the male participants and 3.86 in the female participants. This gender difference was statistically significant with p-value of 0.04. Platelet counts of participants were observed to have low normal value with approximately 25% participants in both the males and females with count <150 x 103/µl. The difference between male and the female platelet counts was statistically significant with the p-value of 0.003.

In our study it was observed that hematological abnormalities had frequent association with PHPT likely in the form of bone marrow involvement leading to anaemia and thrombocytopenia. Also in the systematic review by Pardeep *et al.* [36] after parathyroidectomy significant improvement was observed in anaemia and marrow fibrosis.

In our study the reason for significant difference was attributed to mild-moderate long standing hypercalcemia in females leading to bone marrow involvement leading to cytopenias. On the other hand the acute severe hypercalcemia in the male participants lead to more relative increase in the acute inflammatory markers including NLR.

In line with our observations the study conducted by Lam *et al.* [52] in 2018 observed median Hb revealed of in 13.6g/dl (11.9-14.7) asymptomatic while 12.8g/dl (11.6-13.6) in the symptomatic patients. Similar to our study NLR was observed to have high median value of 2.27. Possible association of thrombocytopenia with PHPT was highlighted in the study by Keukeleire *et al.* [49] in 2017.In their study it was concluded that the haematological abnormalities considered as component of spectrum of factors to guide towards the surgical management especially in asymptomatic patients.

Table 35- The tabular representation of biochemical parameters in the different studies conducted in the esteemed centres of India in last 20 years.

	Institute	**Serum calcium (mg/dl)**	**Serum phosphate (mg/dl)**	**Serum ALP (U/l)**	**Serum PTH (pg/ml)**	**Serum Vit-D3 (ng/ml)**
Current study (2024)	DMCH Ldh	12.3	2.3	196	531.6	25.1
Bhansali *et al.* (2004) [64]	PGI Chd	12.2	2.8	361	809	-
Priya *et al.* (2008) [107]	AIIMS Delhi	12.5	2.5	1086	662	10.2
Gopal *et al.* (2010) [101]	KEM Mumbai	12.6	1.81	762.2	866.6	-
Pardeep *et al.* (2011) [36]	SGPGI Lucknow	12.6	-	1466.5	1005.8	11.6
Maskey *et al.*(2013) [99]	SGR Delhi	12.6	-	756.5	807.7	16.8
Mithal *et al.* (2015) [108]	Medanta Gurgaon	12.2	2.3	872	573.2	18.2
Misgar *et al.* (2016) [38]	Srinagar	12.5	2.2	255.1	377.6	37.2
Arora *et al.* (2021) [9]	DMCH Ldh	11.1	2.5	191.6	210.5	20.67
Thanveer *et al.* (2023) [98]	JIPMER	12.63	2.85	628.8	794.75	15.5

In our study the median albumin adjusted serum calcium was revealed high with the value of 12.3 mg/dl. The calcium levels were observed by Bhansali *et al.* [64] (12.2 mg/dl), Priya *et al.* [107] (12.5 mg/dl), Gopal *et al.*[101](12.6 mg/dl), Pardeep *et al.* [36] (12.6 mg/dl), Maskey *et al.* [99] (12.6 mg/dl), Mithal *et al.*[108](12.2 mg/dl), Misgar *et al.*[38](12.5 mg/dl) and Thanveer *et al.*[98](12.6 mg/dl).

In our study the mean serum calcium level was observed to be higher amongst the males (12.82 mg/dl) than the females (12.03 g/dl). As already discussed males had increased propensity to develop symptoms caused by acute severe hypercalcemia while females had increased propensity to develop symptoms caused by chronic mild-moderate hypercalcemia. The gender difference in serum calcium levels was statistically significant with the p-value of 0.005. This observation was in line with a study conducted by Arora *et al.* [9] where the mean calcium of patients of PHPT without pancreatitis was 11.1 g/dl while PHPT with pancreatitis was 12.24g/dl. The severe hypercalcemia and acute presentation with increased prevalence in the male participants could be correlated.

In our study high PTH was observed with the mean value of 531.6 8 pg/ml. PTH levels assessed in various studies ranged from 210.5 pg/ml (Arora *et al.* [9]) to 1005.8 pg/ml (Pardeep *et al.* [36]). PTH levels were observed by Bhansali *et al.* [64] (809 pg/ml), Priya *et al.* [107] (662 pg/ml), Gopal *et al.* (886.6 pg/ml), Maskey *et al.* [99] (807.7 pg/ml), Mithal *et al.* [108] (573.2 pg/ml), Misgar *et al.* [38] (377.6 pg/ml) and Thanveer *et al.* [98] (794.7 pg/ml).

In our study higher ALP levels were observed with the mean value of 133 U/l. ALP levels assessed in various studies ranged from 191.6 U/l (Arora *et al.*[9]) to 1466.5 U/l (Pardeep *et al.* [36]). ALP levels were observed by Bhansali *et al.* [64] (361 U/l), Priya *et al.* [107] (1086 U/dl), Gopal *et al.* [101] (762.2 U/l), Maskey *et al.* [99] (756.5 U/l), Mithal *et al.* [108] (576.5 U/l), Misgar *et al.* [38] (255.1 U/l) and Thanveer *et al.* [98] (628.8 U/l). ALP levels amongst the female participants (209 U/l) were more than the ALP levels

observed amongst the male participants (175 U/l) .Though the difference was not statistically significant the elevation of serum ALP was attributed to the fact that most of the patients in our study were the elderly females. In the postmenopausal females high ALP levels were observed due to high bone turnover as stated in the study by Mukaiyama *et al.* [109] in 2015.

In our study low Vit-D levels were observed with the mean value of 25.1 ng/dl. Vitamin D levels observed in various studies usually had value <30 ng/dl. Vitamin D levels were assessed by Priya *et al.* [107] (10.2 ng/dl), Pardeep *et al.* [36] (11.6 ng/dl), Maskey *et al.* [99] (16.8 ng/dl), Mithal *et al.* [108] (18.2 ng/dl), Arora *et al.*[9] (20.7 ng/dl) and Thanveer *et al.*[98] (15.5 ng/dl). Concomitant hypovitaminosis-D was attributed to more severe symptomatic presentation of PHPT in Indian population.[99]

In our study hypophosphatemia was observed with the mean phosphate level of 2.3 mg/dl. Similar lower phosphate levels were observed in the studies by Bhansali *et al.* [64] (2.8 mg/dl), Priya *et al.* [107] (2.5 mg/dl), Gopal *et al.* [101] (1.8 mg/dl), Mithal *et al.* [108] (2.3 mg/dl), Misgar *et al.* [38] (2.2 mg/dl), Arora *et al.*[9] (2.8 mg/dl) and Thanveer *et al.* [98] (2.5 mg/dl). This observation can be attributed to the physiological action of PTH on proximal convoluted tubule leading to decreased phosphate reabsorption and increased urinary phosphate excretion.

In our study high uric acid levels were observed with the mean level of 6.1mg/dl. Higher level was observed amongst the male participants (6.2 mg/dl) than the female participants (5.9 mg/dl). In other studies positive correlation of uric acid was highlighted with serum PTH levels. [110]

In our study 24 hour urinary calcium was observed with a high value of 239.98 mg/dl. 24 hour urinary calcium amongst males (251.4±61.1 mg/24 hours) was higher as compared to the females (233±61.9 mg/dl). More than 70% study participants had urinary calcium of >200 mg/dl while severe hypercalciuria (>400 mg/dl) was seen only in 2 male participants.

The finding of more hypercalciuria amongst the males was associated with higher tendency of male patients to develop renal calculi. This finding is in line with observation of the study by Aggarwal *et al.* [111] in 2021 which concluded young age and male gender as the predictors of renal involvement in PHPT.

Hence the conclusions that were drawn from the observations include low hemoglobin, high NLR, thrombocytopenia, high ALP, high PTH, hyperuricemia and hypophosphatemia in the patients with PHPT. Gender differences which were observed in biochemical studies included statistically significant lower Hb and platelet levels in the female participants. Statistically significant higher serum calcium and NLR in the male participants were also observed. High urinary calcium levels were observed more commonly in the male participants which can be considered as a risk factor for renal calculi formation. However other biochemical investigations did not have any significant gender difference.

PHPT was observed to have increased cardiovascular mortality and morbidity. In our study ECHO findings revealed systolic dysfunction (26.4%), diastolic dysfunction (45.9%), PH (42.4%), LVH (54%) and AVC (19.5%). It was observed that in cardiac assessment the male participants showed more systolic dysfunction, PH and LVH while the female participants showed more diastolic dysfunction and AVC. In our study cardiac involvement was observed with higher prevalence than usual. However in our study significant prior comorbidities were also present which are also the known risk factors for cardiac involvement. Hence this cardiac morbidity documented was not solely attributed to PHPT.

In PHPT cardiac observations were made in very less number of studies. Purra *et al.* [53] in 2022 in a study compared patients and controls for cardiac involvement in PHPT. It was concluded that symptomatic PHPT patients tend to have substantial cardiac structural and functional abnormalities including elevated LVMI, diastolic dysfunction, and valvular,

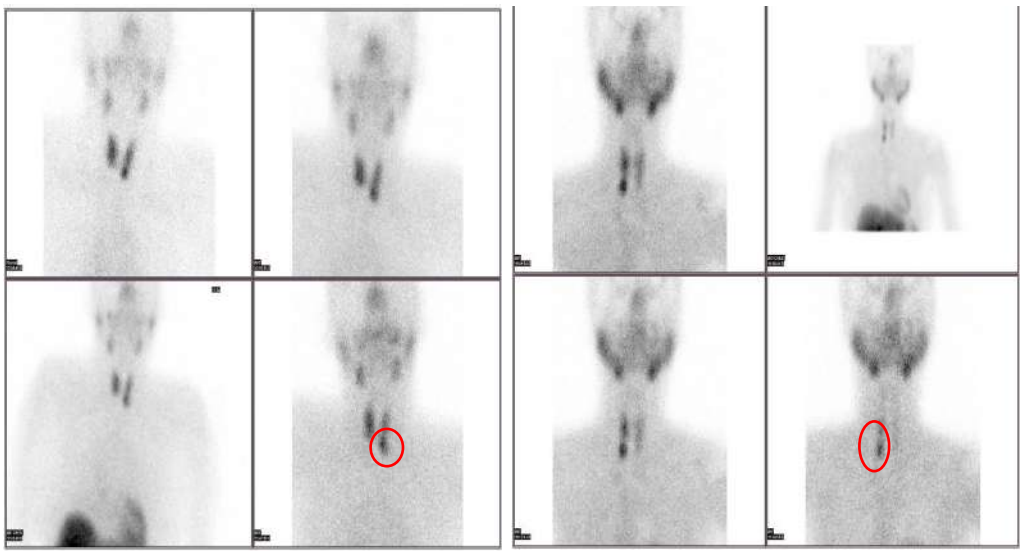
septal and myocardial calcium depositions. Similar to the findings of our study the observations of the study by Purra *et al.*[53] included median LVMI of 90.95g/m2 suggestive of LVH, E/A ratio of 0.98 suggestive of diastolic dysfunction and 29% patients with AVC suggestive of ectopic calcifications. In their study serum PTH, calcium and uric acid were significantly correlated with calcifications and also serum calcium showed negative correlation with E/A ratio.

In our study the preoperative localisation of parathyroid adenoma was done by USG-Neck and Tc-99 sestamibi spect scan. The preoperative localisation by USG-Neck was obtained in 83.4% of the investigated participants with sensitivity of 83.5% and specificity of 33.3%. It was observed that the preoperative localisation by Tc-99 sestamibi spect scan was seen in 88.9% of the investigated participants with sensitivity of 96.9% and specificity of 66.7%. By Bhansali *et al.* [64] and Pardeep *et al.* [36] the sensitivity of USG was observed as 65-77% while the sensitivity of Tc-99 spect was observed as 87-100%. In the series by Misgar *et al.* [38] sensitivity of USG-Neck and Tc-99 was 89.5% and 95.3% respectively. Also in a study by Arora *et al.* [9]) ultrasonographic interrogation revealed parathyroid adenoma in 66.6% of the study participants and technetium sestamibi scan localised parathyroid adenoma in 83.3%.

It was observed that with the sensitivity of 83.5% the simple technique of ultrasonography if performed by vigilance can act as effective first line screening. However the reported sensitivity of USG in Indian studies is low which can be attributed to absence of dedicated parathyroid sonologists. Tc-99 sestamibi spect scan remains superior in terms of pre-op detection. It was observed that USG-neck showed more evidence of parathyroid adenoma in the male participants as compared to the female participants. Rest of the radiological assessment did not show any gender variation.

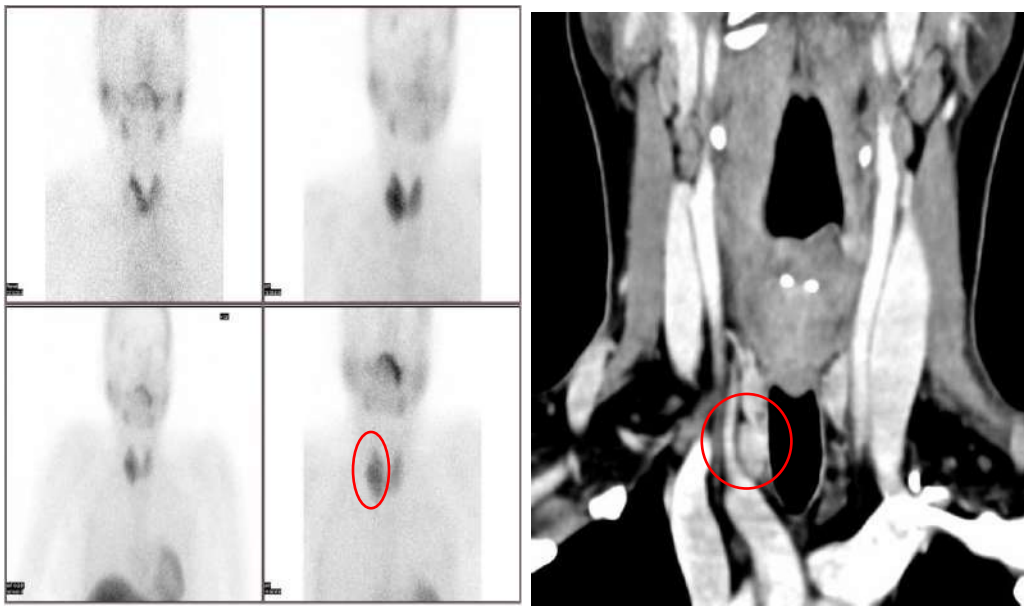
Figure 42- Pictorial representation of a 54 year old female with ultrasonographic evidence of parathyroid adenoma (Patient-67)

In our study parathyroid adenoma was present in left lower parathyroid gland in 46 patients (44.2%), right lower parathyroid gland in 45 patients (43.3%), left upper parathyroid gland in 3 patients (2.9%) and right upper parathyroid gland in 4 patients (3.8%). In rest of the 6 patients (5.8%) ectopic parathyroid adenoma was localised. It was observed that parathyroid adenoma was more common in the inferior glands as compared to the superior glands. Similar findings were also highlighted in various studies like Arora *et al.* [9] LIPA was seen in 26.6%, RIPA was seen in 16.6%, LSPA was seen in 13.3% and RSPA was seen in 10% patients. More frequent involvement of left inferior glands was also seen in another study by Jha *et al.* [100].



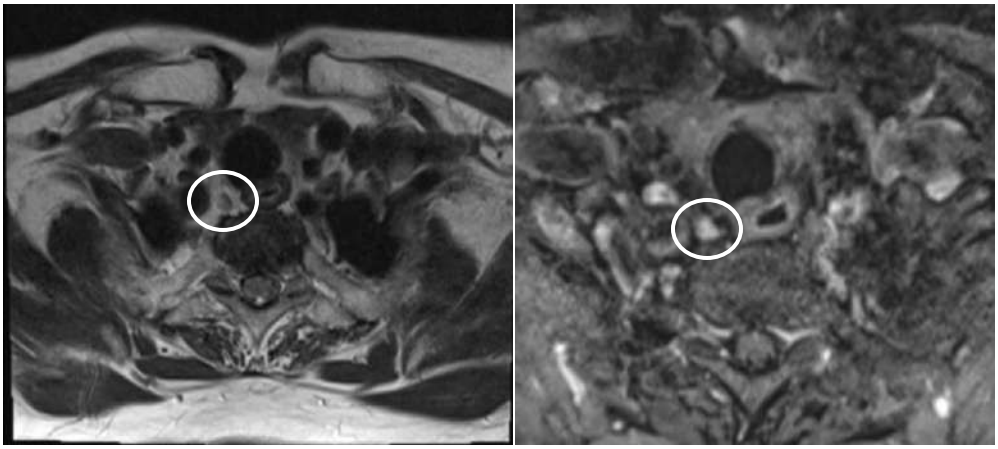
A B

Figure 43- Pictorial representation Tc-99 sestamibi spect scan A. Left Inferior Parathyroid Adenoma B. Right Inferior Parathyroid Adenoma [Parathyroid gland (encircled) showing persistent delayed enhancement beyond 60 mins]



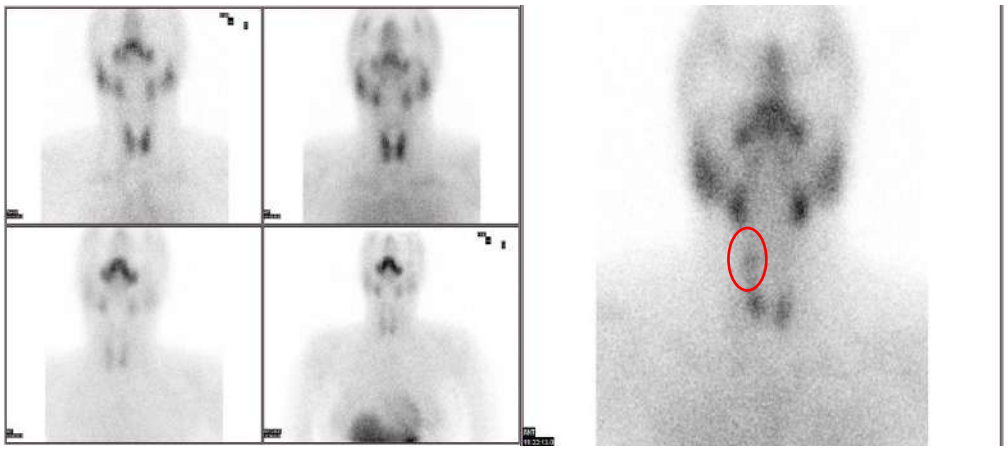
A B

Figure 44- Pictorial representation of A.Tc-99 sestamibi spect scan showing a large RIPA (Patient-22, a 57 year old female), B. Computed Tomography-neck showing RIPA (Patient-47, a 47 year old male)



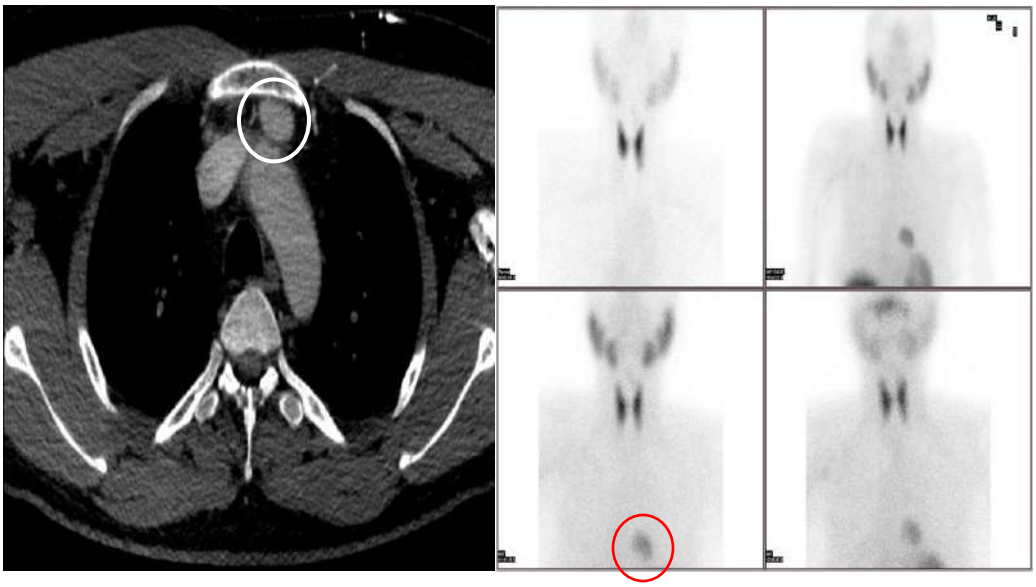
A **B**

Figure 45- Magnetic resonance imaging as diagnostic modality for parathyroid adenoma A.T2 weighted image showing hypodense lesion on right side and inferior aspect of thyroid suggestive of RIPA B. Post contrast image of the same lesion.



A. **B.**

Figure 46- A. Pictorial representation of normal technetium sestamibi spect scan imaging (Patient-11), 46 y/o/ female had clinical suspicion of PHPT with USG- neck revealing hypoechoic right inferior lesion. Due to negative Tc-99 spect, PET-CT was done for pre-operative localisation which suggestive of RIPA **B. Showing Tc-99 sestamibi suggestive of RSPA (less prevalent lesion) in a 58 y/o/ female (Patient-23)**



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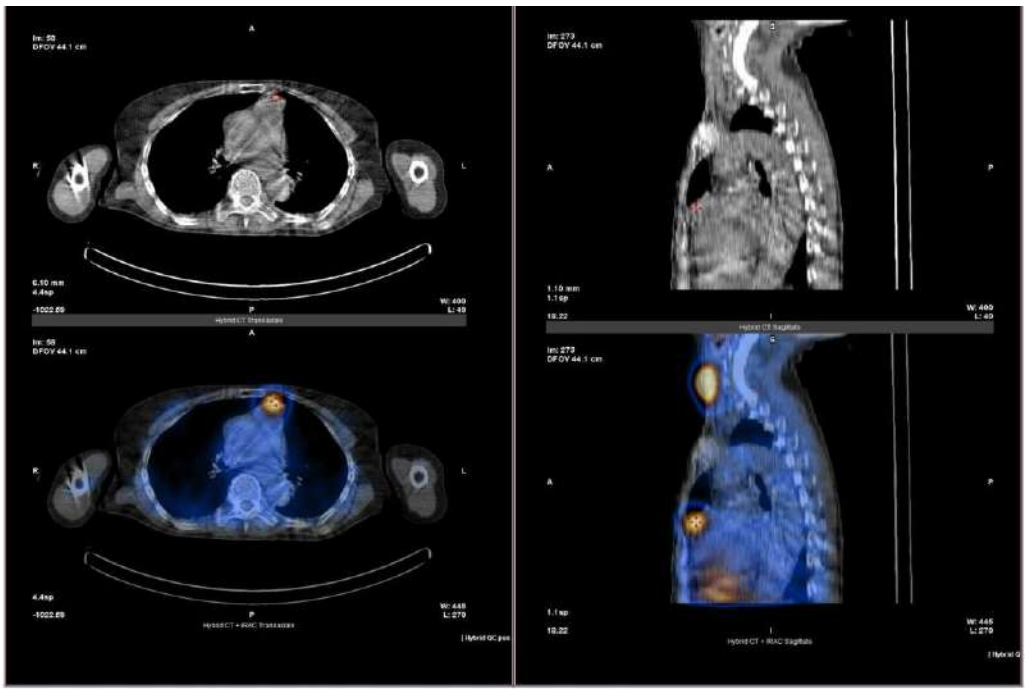
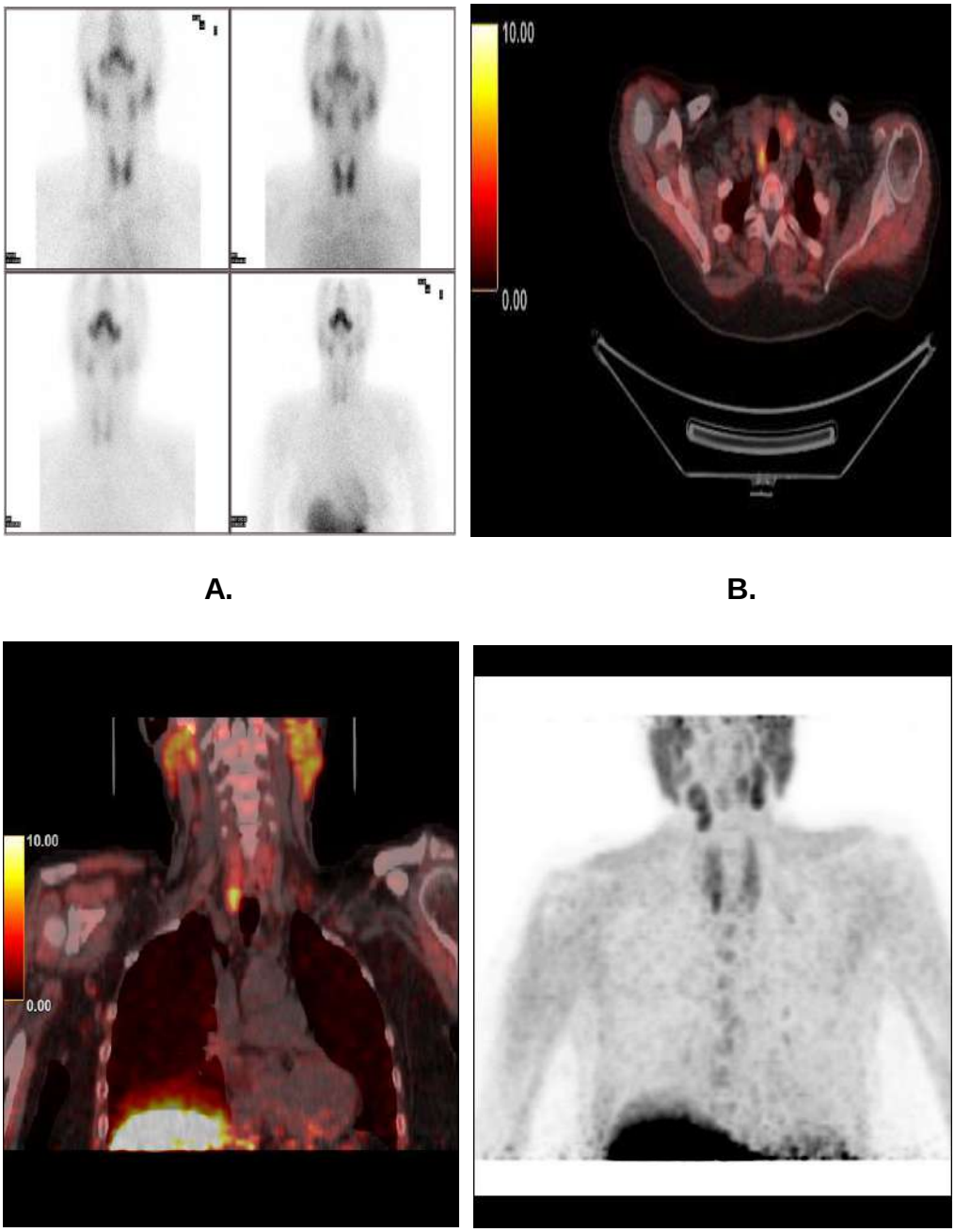


C

Figure 47- Pictorial representation of ectopic parathyroid adenoma A. Computed Tomography showing anterior mediastinal mass B. Technetium scan showing anterior mediastinal mass with persistent delayed enhancement C. Spect imaging showing yellow enhancing mass suggestive of ectopic parathyroid adenoma localised to anterior mediastinum

In our study 11 patients did not undergo Tc-99 sestamibi spect scan. Out of these 11 patients PET-CT was done in one patient which was suggestive of RIPA and CT-neck was done in 3 patients which localised adenoma. Out of 13 Tc-99 negative patients, they were subjected to CT-neck which showed RIPA in 1 patient while CT-neck was non-significant in 1 participant. 1 patient underwent MRI-neck and 1 patient underwent PET-CT, both were suggestive of RIPA. Out of 13 Tc-99 negative patients, 11 patients had ultrasonographic evidence while 2 patient did not show any USG lesion as well.



A. B.

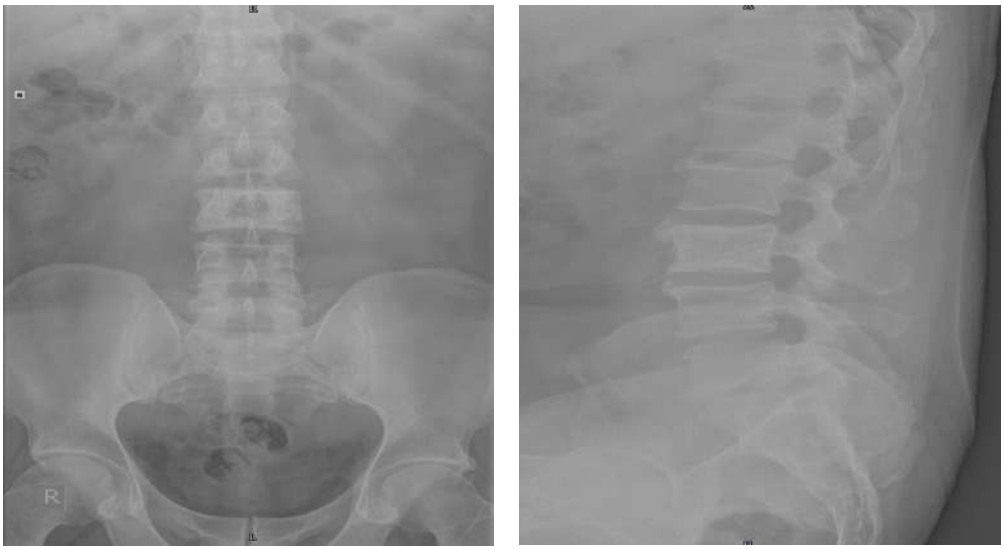
C. D.

Figure 48- PET- choline imaging based diagnosis of a patient (patient- 10), 63 year old female with the clinical suspicion of PHPT with no imaging evidence on Tc-99 sestamibi spect scan. Choline-PET was done which revealed RIPA.

In our study to observe the radiological evidence of bony involvement, X-ray B/L hands, skull or spine showed the evidence of PHPT in 31.9% of the study participants.

A

B



C. D.

E.

Figure 49- Roentogenographic imaging showing skeletal survey A. Hands (AP and Lateral views) B. Spine (AP and Lateral views) C. Skull (AP and Lateral views) D. Foot E. Knees (AP and Lateral views)

Abnormal skeletal findings-

Figure 50- Roentogenographic imaging of hands- showing sub periosteal bone resorption especially proximal and middle phalanges of 2nd and 3rd fingers

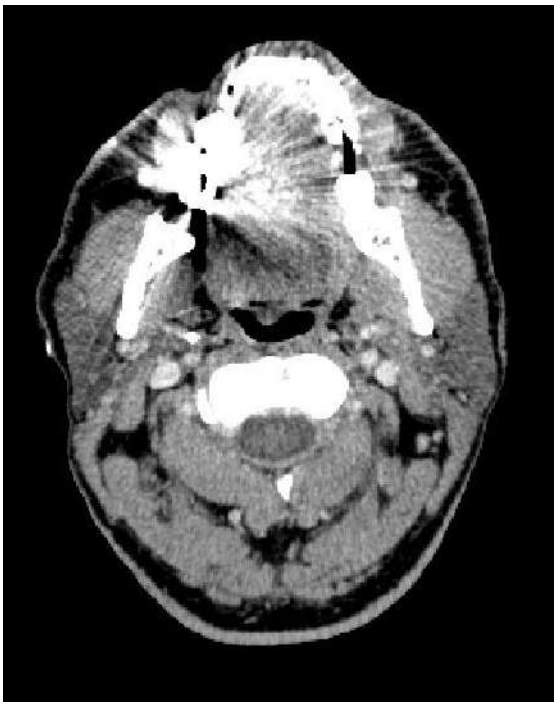


Figure 51- CT representation of Brown Tumour- on examination patient also had jaw swelling

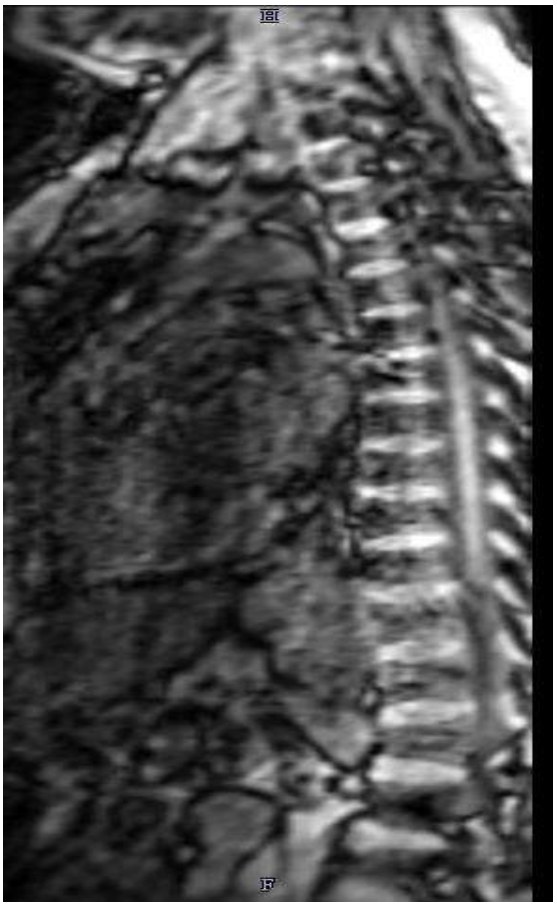


Figure 52- Pictorial representation of MRI spine showing parathyroid spinal osteodystrophy

Figure 53- Roentogenographic imaging evidence of spinal involvement- Ruger Jersey spine

In our study USG-W/A observed various findings associated with PHPT. USG-W/A revealed acute pancreatitis (20.6%), renal calculi (20.6%) and chronic pancreatitis (5.9%). Pancreatitis was more commonly observed in the male population and the similar male preponderance in pancreatitis was also highlighted in the study by Arora *et al.* [9].

Figure 54- Pictorial representation of CT imaging of Acute Pancreatitis (Patient 1)

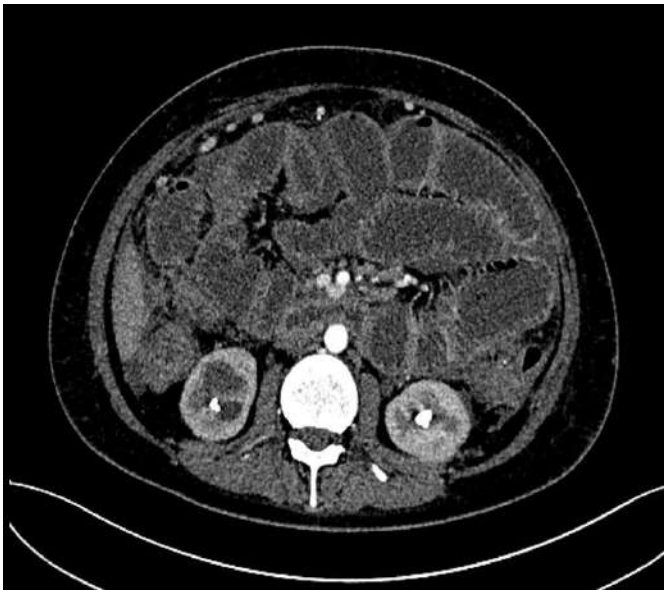


Figure 55- Pictorial representation of CT imaging of B/L nephrolithiasis (Patient-39)

4. Treatment:

In our study it was observed that more number of the female participants (29.6%) were treated on the OPD basis than the male participants (21.3%). The probable reason attributed to this was mild-moderate hypercalcemia with less severe symptoms amongst the females or the decreased health care facilities available for female Indian population.

In the admitted patients surgery is offered to all the patients considering definitive and curative nature of the intervention. Pharmacological therapy was used if patient was unfit for surgery due to medical comorbidities or patient was unwilling for the intervention. All the admitted patients were started with medical therapy for acute stabilisation before undergoing surgical intervention.

In our study the most common initial modality used was IVF hydration with loop diuretics (in 88.3% of the admitted patients). Infusion rate was titrated according to fluid status of the patient, prior comorbidities and the age of patient. Loop diuretics were added after intravascular fluid restoration. After IVF hydration decrease in serum calcium levels was observed in all the patients. However serum calcium levels did not return to normal value. Similar findings were observed by Oueslati *et al.* [112] where IVF infusion was administered for 3.1±1.7 days with mean serum calcium difference of 1.08 mg/dl. In their study it was observed that addition of furosemide rather lead to increased serum calcium levels. It was concluded from their study that intravascular fluid restoration is most important first step prior to diuresis.

In our study calcitonin was the second most common (86.2%) modality used in the dose of 100 U every 6- 8 hourly. Prompt reduction in the serum calcium levels was observed. Continuation of drug beyond 48-72 hours was not associated with any significant benefit due to tachyphylaxis by calcitonin receptor downregulation.

In our study the next common drug used was cinacalcet in 75.5% of the treated patients. Cinacalcet has calcimimetic action by acting on CaSR receptors thus decreases the PTH secretion [93]. These findings are in line with the review done which was associated with normalisation of serum calcium and PTH in >90% of the study participants.[94] In a study by Misiorowski *et al.* [113] normalisation of calcium was observed in 55% with decreased serum calcium levels in 83% of the participants after cinacalcet administration.

In our study most of the patients responded to above mentioned modalities. For persistent non-responding hypercalcemia next options were explored. In 46.8% (n=44) of the admitted participants zoledronate was used as 4mg infusion. Significant serum calcium reduction was reported in several studies. Initial fall has been reported to last for more than 6 months.[87] A large double-blinded RCT after zoledronate administration observed significant BMD improvement with static serum calcium, urinary calcium and PTH levels. [91] In the study by Oueslati *et al.* [112] it was observed that zoledronic acid infusion administration lead to normalisation of calcium in 60% patients.

In the patients with renal involvement zoledronate was contraindicated. In cases with persistent non-responding hypercalcemia denosumab 120 mcg was administered subcutaneously. In our study denosumab was administered to 12.8% (n=12) of the admitted patients. Various studies have highlighted the role of denosumab in increasing BMD and decreasing ALP over 1-2 years of therapy. [92]

In our study zoledronate was administered more commonly amongst the female participants (56.1%) than the male participants (32.4%). This observation was attributed more prevalence of renal involvement amongst the male participants contraindicating the use of zoledronate. It also justifies the more frequent use of denosumab amongst the male participants (13.5%) than the female participants (12.3%). In our study the

patients with severe life threatening hypercalcemia (5.3%) were dialysed. Indication of hemodialysis was arrhythmias in two patients with neurologically altered sensorium in three patients.

Denosumab decreases bony resorption by preventing RANKL binding to RANK receptor. In a study by Eremkina *et al.* [114] ten patients were observed and denosumab was considered as a very important tool to buy time before surgery or in patients in whom surgery was contraindicated. In their study the trend of calcium reduction by third day followed by below normal level on seventh day was observed. Along with significantly decreased serum calcium levels, improvement in eGFR was also observed on day 7.

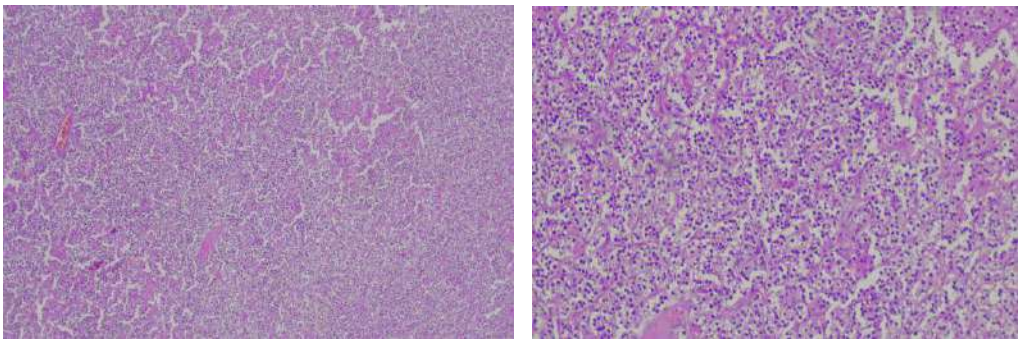
In our study another observation which was highlighted included the more frequent non-responding hypercalcemia in the female participants. Though the female participants have mild-moderate hypercalcemia but the chronicity associated probably makes reversal stubborn.

In our study mean number of days to normalisation of calcium were observed as 8.9 days. After hospitalisation females had longer duration (9.1 days) to normalisation of serum calcium levels than the male participants (8.4 days). The mean duration to normalisation of calcium after zoledronate or denosumab ranged from 3.5-4.5 days. In the study by Oueslati *et al.* [112] the average duration to lowest serum calcium was 6±3.9 days.

In our study 81.9% of the admitted patients were surgically operated constituting 89.2% of the admitted male participants and 77.1% of the female participants. Again the reason attributed was either the chronic mild-moderate nature of hypercalcemia with less severe symptoms amongst the female participants or the less health care facilities available for Indian females.

In our study post parathyroidectomy lowering of calcium levels was observed in all the patients. Persistent hypocalcemia of <8.4 mg/dl beyond 2-4 days was noted due to HBS (Hungry Bone Syndrome) in 10.6% of the operated patients. In the Indian text HBS has been observed in 24% to 82% of the cases [47]. Our observations are in line with a study conducted by Misgar *et al.* [38] where HBS was observed in 10.12% of their study participants. The probable reason for lower prevalence of HBS in our study was probably due to early use of high dose calcium and calcitriol supplements. Some patients had very severe symptomatic hypocalcemia requiring intravenous calcium supplementation. One patient even succumbed to post-operative severe hypocalcemia.

In our study the biopsy sample was sent for histological analysis. The samples analysed had mean weight of 7.1±5.3g (range= 0.2-29 g) with mean size of 2.4x1.5x0.7 cm. The most common observation was parathyroid adenoma (84.4%). Parathyroid carcinoma was rare observation (7.8%). Histopathological specimens remained inconclusive in 7.8% patients. The systematic review by Pardeep *et al.* [36] stated that the developed countries (2-4 g) usually had lower mean tumour weight in comparison to the developing countries (1.25-102 g). In the review prevalence of adenoma was 89.1% and carcinoma was 4.37%. Various series reported carcinoma prevalence between 2.6-6%.[36] However the higher prevalence of carcinoma in our study can probably be attributed to our institute being tertiary institution with the well-established super-speciality oncology centre catering more patients from all over North India.



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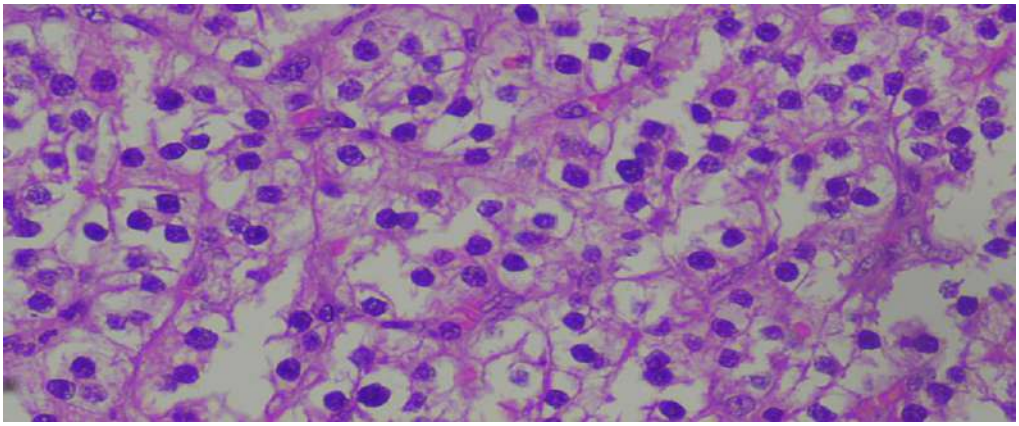
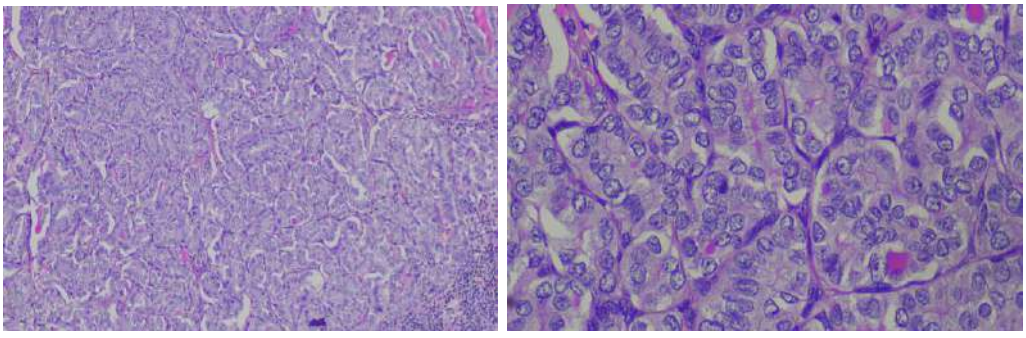


C

Figure 56- Pictorial depiction of parathyroid adenoma- chief cells and oncocytic cells A. 10 X magnifying power B. 40 X magnifying power C. 100 X magnifying power



A B

Figure 57- Pictorial depiction of parathyroid carcinoma- A. Low power view 40X B. High power view 100 X (bizarre cells with nuclear atypia and nucleolar predominance)

In our study it was observed that mortality associated with PHPT was 2.3%. The mortality was attributed to post-op hypocalcemia in one patient and arrhythmias in rest of the two patients. In the study by Hedback *et al.* [115] the risk ratios for death from cardiovascular disease were 1.71 for male and 1.85 for female patients. In their study it was concluded that the adenoma weight, serum calcium levels and PTH levels were predictive of risk of death. It was also concluded in their study that surgical intervention provides relief of symptoms and also decreases morbidity and mortality.

In our study 92.2% patients were followed up with serum calcium and serum PTH. The mean serum calcium was observed as 9.05±0.86 mg/dl with mean PTH level of 31.03±87.4 pg/ml.

SUMMARY & CONCLUSION

SUMMARY

The present study aimed to evaluate the clinical profile of patients presenting with primary hyperparathyroidism in tertiary care hospital. After reviewing and analysing the possible aspects, the following points were summarised:

Demographic data:

- In our study total of 128 patients were enrolled
- Females were more commonly affected with the male: female of 1:1.7. More than 2/3rd patients were females. Female gender was found to be a significant risk factor for PHPT.
- The mean age at diagnosis was 53.3±14.2 years. More than 2/3rd of the female participants presented above 50 years of age. Male participants had bimodal presentation at 31-40 years and 61-70 years and females had peak presentation from 51-70 years.
- It was observed that PHPT is predominantly diagnosed in elderly population. Hence PHPT is a disease with elderly female preponderance. However if present in the males the presentation was relatively younger.
- Mean duration of symptoms prior to diagnosis in our study was 24.03±17.7 months. Due to increased awareness and routine testing this duration is gradually declining with time.
- The male participants were more often diagnosed within 2 years however amongst the female participants delayed peak in diagnosis and 25% patients were diagnosed in the third year of symptom onset.

Clinical presentation and examination:

- Calcium being vital element with its involvement in multiple physiological processes, the patients with PHPT had multisystem presentation with varied symptoms.
- In the pentad the relative prevalence was observed as:
  Bony involvement (44.1%) >Gastrointestinal (43.4%) >Neuropsychiatric (40.6%) >Renal (31.3%) >Asymptomatic (16.4%).
- Renal, gastrointestinal and neuropsychiatric manifestations were more common amongst the male participants than in the female participants. However the bony involvement and asymptomatic presentation were more common amongst the female participants than the male participants.
- The pattern of symptoms was observed amongst the different genders on critical analysis. The male participants had severe symptoms at presentation including neuropsychiatric manifestations, acute pancreatitis and renal stones. On the other hand the females had predominance of mild-moderate symptoms at presentation including bony pains and chronic pancreatitis or even the asymptomatic presentation.
- In the patients with PHPT increased prevalence of prior comorbidities DM (50%), HTN (50%), CAD (14.1%) and CVA (16.4%) were observed. On examination patients predominantly had systolic hypertension.
- In our study on examination jaw swelling (6.3%), predominant proximal myopathy (52.3%) and mild-moderate mental impairment (35.9%) on MMSE was observed.

- It was observed that psychological distress was more common in the male participants than the female participants. However more female participants had severe psychological distress than the male participants. Almost 1/4th of the females had severe psychological distress

Investigational assessment

- PHPT patients had low hemoglobin, high NLR and low platelet levels. Patients also had high ALP, high corrected serum calcium, high PTH, hyperuricemia and high 24hr urinary calcium. Hypovitaminosis-D and hypophosphatemia were also observed in the study population.
- In our study statistically significant lower Hb level and platelet levels were observed in the female participants in comparison to the male participants. Also statistically significant high NLR value was observed in the male participants than the female participants.
- Another important observation that was made was statistically significant difference in the mean values of corrected serum calcium levels amongst the males and the females with the p-value of 0.005. It was observed that higher mean calcium was observed in the males. Also the high urinary calcium level was observed more commonly in the male participants which can be considered as a risk factor for renal calculi formation. However other biochemical investigations did not have any significant gender difference.
- PHPT was observed to have increased cardiovascular mortality and morbidity. In our study ECHO findings revealed systolic dysfunction (26.4%), diastolic dysfunction (45.9%), PH (42.4%), LVH (54%) and AVC (19.5%).
- The preoperative localization by USG-Neck was obtained in 83.4% of the investigated participants with sensitivity of 83.5% and specificity of 33.3%. The preoperative localization by Tc-99

sestamibi spect scan was seen in 88.9% of the investigated participants with sensitivity of 96.9% and specificity of 66.7%.

- Localization of parathyroid adenoma from most to least common was LIPA (44.2%), RIPA (43.3%), ectopic (5.8%), RSPA (3.8%) and LSPA (2.9%). It was observed that parathyroid adenoma was more common in the inferior glands as compared to the superior glands.
- Radiological evidence of bony involvement was observed by X-ray B/L hands, skull or spine were done, which showed the evidence of PHPT in 31.9% of the study participants.
- USG-W/A observed various findings associated with PHPT. USG-W/A revealed acute pancreatitis (20.6%), renal calculi (20.6%) and chronic pancreatitis (5.9%). Acute pancreatitis and renal calculi was more commonly observed in the male population. Chronic pancreatitis and renal parenchymal changes were more commonly observed in the female population.

Treatment

- Most to least common treatment modality used in the admitted patients included IVF hydration (88.3%), diuretics (88.3%), calcitonin (86.2%), cinacalcet (75.5%), zoledronate (46.8%), denosumab (12.8%) and hemodialysis (5.3%).
- Persistent and non-responding hypercalcemia was more commonly observed in the female participants requiring use of zoledronate and denosumab.
- Use of zoledronate was more common in the female participants and the use of denosumab was more common in male participants.
- Mean number of days to normalization of calcium after hospitalization were 8.9±3.7 days.

- Mean number of days to normalization of calcium after zoledronate were 3.6±1.3 days.
- Mean number of days to normalization of calcium after denosumab were 3.9±0.9 days.
- 81.9% of the admitted patients were surgically operated and 10.6% of the operated patients had HBS. The mean size of excised adenoma was 2.4x1.5x0.7cm. The mean weight of excised adenoma was 7.1±5.3 g.
- Histopathological analysis of post-surgery sample showed parathyroid adenoma (84.4%) > parathyroid carcinoma (7.8%) > inconclusive (7.8%). It was observed that histologically parathyroid adenoma was much more common than the parathyroid carcinoma.

Follow up

- On follow up the mean serum calcium levels were observed as 9.05±0.86 g/dl and the mean PTH levels were observed as 31.03±87.4 pg/ml
- PHPT was associated with 2.3% mortality.

CONCLUSIONS

Primary hyperparathyroidism is the disease with elderly female preponderance characterized by hypercalcemia and raised PTH levels. Though the disease was significantly more common amongst the female participants but the hypercalcemia amongst the male participants was relatively more severe leading to severe symptoms and acute presentation. The severe symptoms with male preponderance include acute pancreatitis and renal calculi. Due to severe hypercalcemia more renal calcium excretion, evident by severe hypercalciuria, occurs in the male participants acting as a potent risk factor for renal calculi formation. On the other hand females had mild-moderate hypercalcemia with non-severe symptom presentation leading to relatively delayed diagnosis. The non-severe symptoms with female preponderance include bony pains, chronic pancreatitis or even the asymptomatic presentation.

The pictorial represents (Figure 58):

1. More area under green curve signifying more predominance of the disease in the female patients.
2. Higher peak in the orange curve signifying more hypercalcemia and hypercalciuria amongst the male participants and also the more severe presentation in the form of acute pancreatitis and renal calculi.
3. The early peak in the orange curve depicts duration to diagnosis which is less amongst the male participants, the severity of symptoms lead to early diagnosis.
4. The delayed normalization of serum calcium levels is depicted in the female participants emphasizing the stubbornness and increased use of zoledronate or denosumab.

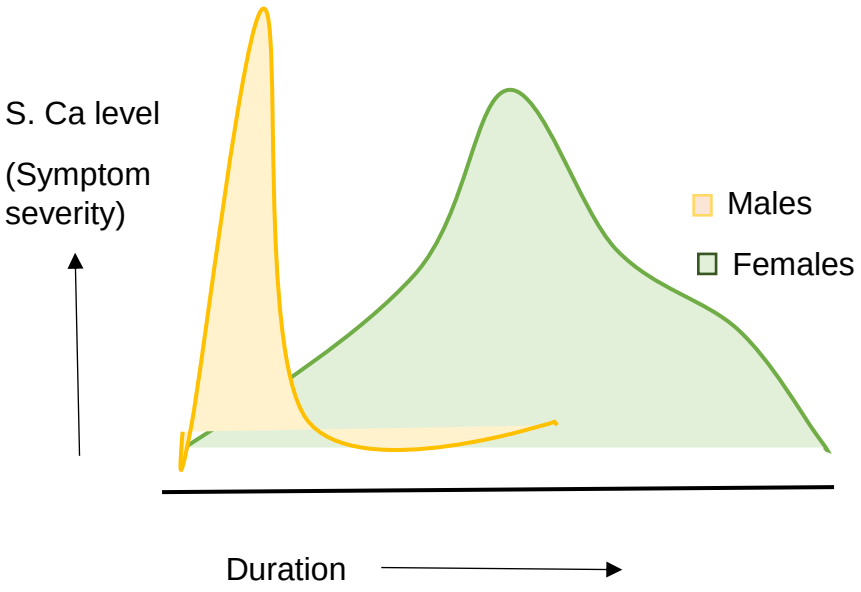


Figure 58- Pictorial representation of gender-based difference in serum calcium (symptom-severity) and duration of illness prior to diagnosis.

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Key to Master Chart

S. no.	Variable	Represents	Assessment
1	S_NO	Enrollment number of the patient	Demography
2	NAME	Name of the patient enrolled	
3	ID	Unique institute identity number	
4	AGE	Age of the patient at time of diagnosis	
5	SEX	Gender of the enrolled patient 1=MALE 2=FEMALE	
6	DURA_M	Duration of symptoms prior to diagnosis in months	History
7	HEMAT_U	Hematuria as symptom 1=PRESENT 2=ABSENT	
8	POLY_U	Polyuria as symptom 1=PRESENT 2=ABSENT	
9	R_STONES	Renal stones as symptom 1=PRESENT 2=ABSENT	
10	B_PAINS	Bony pains as symptom 1=PRESENT 2=ABSENT	
11	FRACTURE	Fracture as symptom 1=PRESENT 2=ABSENT	
12	P_ABD	Pain abdomen as symptom 1=PRESENT 2=ABSENT	
13	CONST_N	Constipation as symptom 1=PRESENT 2=ABSENT	
14	DEPRES_N	Depression as symptom 1=PRESENT 2=ABSENT	
15	ANXIETY	Anxiety as symptom 1=PRESENT 2=ABSENT	
16	NO_SYMP	Asymptomatic presentation 1=PRESENT 2=ABSENT	
17	DM	Past history of diabetes 1=PRESENT 2=ABSENT	Past History
18	HTN	Past history of hypertension 1=PRESENT 2=ABSENT	
19	CAD	Past history of CAD 1=PRESENT 2=ABSENT	
20	CVA	Past history of CVA 1=PRESENT 2=ABSENT	
21	SBP	Systolic blood pressure reading of patient	Examination
22	DBP	Diastolic blood pressure reading of patient	

23	HR	Heart rate reading of patient	
24	JAW_SW	Jaw swelling on examination 1=PRESENT 2=ABSENT	
25	DIS_PW	Distal muscle power Values=0,1,2,3,4,5	
26	PROX_PW	Proximal muscle power Values=0,1,2,3,4,5	
27	MMSE	Minimental status examination score Values=0→30	
28	PHQ-4	PHQ-4 score Values=0→12	
29	HB	Hemoglobin in CBC of the patient	Biochemical investigations
30	NLR	Neutrophil to lymphocytic ratio in CBC of the patient	
31	PLT	Platelets in CBC of the patient	
32	ALP	Alkaline phosphate levels in LFT of the patient	
33	ALB	Albumin levels in LFT of the patient	
34	CA	Serum calcium level of the patient	
35	C_CA	Corrected albumin adjusted serum calcium level of the patient	
36	PTH	PTH level in the lab investigations of the patient	
37	VITD	Vitamin-D level in the lab investigations of the patient	
38	PHOS	Phosphate level in the lab investigations of the patient	
39	UA	Uric acid level in the lab investigations of the patient	
40	AMYLASE	Amylase level in the lab investigations of the patient if done	
41	LIPASE	Lipase level in the lab investigations of the patient if done	
42	U_CA	24 hr urinary calcium level of the patient	
43	EF	Ejection fraction noted on echocardiography of the patient	Cardiological assessment
44	FS	Fractional shortening noted on echocardiography of the patient	
45	E	Peak early diastolic velocity across mitral valve on echocardiography of the patient	
46	A	Peak late diastolic velocity across mitral valve on echocardiography of the patient	
47	E/A	Emax/Amax ratio obtained as E/A (value 45/ value 46)	

48	E_IVST(D)	Echocardiographic interventricular septal thickness (diastolic) (in cm)	
49	E_LVID(D)	Echocardiographic left ventricular internal diameter (diastolic) (in cm)	
50	E_LVPW(D)	Echocardiographic left ventricular posterior wall thickness (diastolic) (in cm)	
51	LVMI	Left ventricular mass index Calculated by: Formula 1 Anatomic LVM = 0.8 {1.04 ([LVID + PWT + IVST] ^{3} – [LVID] ^{3})} +0.6 g (*taking LV dimension in cm)* LVMI= LVM/BSA (BSA=1.7 m^2)	
52	PASP	Pulmonary arterial systolic pressure noted on echocardiography of the patient	
53	AVC	Aortic valve calcification noted on echocardiographic study of the patient 1=PRESENT 2=ABSENT	
54	X_RAY	Roentogenographic skeletal survey for bony involvement in the patient 1=PRESENT 2=ABSENT Blank=NOT DONE	Radiological assessment
55	USG_NECK	Parathyroid hypoechoic lesion on ultrasonography of the patient 1=PRESENT 2=ABSENT Blank=NOT DONE	
56	TC99	Parathyroid lesion on Tc-99 sestamibi spect scan localization RIPA=Right inferior parathyroid adenoma LIPA= Left inferior parathyroid adenoma RSPA=Right superior parathyroid adenoma LSPA= Left superior parathyroid adenoma ECTOPIC=Ectopic parathyroid adenoma 2= Lesion not localized Blank= Tc-99 sestamibi spect not done in the patient.	
57	USG_WA	Abdominal ultrasonographic findings of the patient AP=Acute pancreatitis CP=Chronic Pancreatitis RPC=Renal parenchymal changes RC=Renal calculi NS=Non significant Blank= Investigation not done	

58	PT_MODE	Mode of patient presentation 1=OPD 2=IPD	Medical treatment
59	IVF	Treatment offered with intravenous fluid hydration 1=YES 2=NO Blank=OPD	
60	FUROSE	Treatment offered with loop diuretic furosemide 1=YES 2=NO Blank=OPD	
61	CALCITO	Treatment offered with calcitonin 1=YES 2=NO Blank=OPD	
62	CINACAL	Treatment offered with cinacalcet 1=YES 2=NO Blank=OPD	
63	ZOLEDRO	Treatment offered with infusion zoledronic acid 1=YES 2=NO Blank=OPD	
64	DENOSU	Treatment offered with denosumab 1=YES 2=NO Blank=OPD	
65	HD	Treatment offered with hemodialysis 1=YES 2=NO Blank=OPD	
66	CA_NOR_H	Number of days to normalization of calcium after hospitalization (days)	
67	CA_NOR_Z	Number of days to normalization of calcium after zoledronate (days)	
68	CA_NOR_D	Number of days to normalization of calcium after denosumab (days)	
69	SURGERY	Surgical intervention in the patient 1=DONE 2= NOT DONE	Post-surgical intervention and histological profile
70	HBS	Hungry bone syndrome observed in the operated patients 1= YES 2=NO Blank= Patient not operated	
71	HBSCA	Lowest serum calcium level noted in patient with HBS in mg/dl	
72	HIS_SZ_A	Histology sample size largest dimension (in cm) in operated patients	
73	HIS_SZ_B	Histology sample size middle dimension (in cm) in operated patients	
74	HIS_SZ_C	Histology sample size smallest dimension (in cm) in operated patients	
75	HIS_WT	Histology sample size weight (in g) in operated patients	
76	HIS_S/O	Histopathological biopsy assessment report in the operated patients PA=Parathyroid adenoma PCA=Parathyroid carcinoma INC=Inconclusive	
77	OUTCOME	Outcome of the patients at follow up assessed once between 1-6 months after enrollment FU=Followed patients	Outcome

		LTFU=Lost to follow up (Attrition bias) EXP= Expired patients	
78	FU_CA	Follow up serum calcium levels in the patients at follow up once between 1-6 months (in mg/dl)	
78	FU_CCA	Follow up corrected serum calcium levels (taking average albumin as 3.7 mg/dl) at follow up once between 1-6 months (in mg/dl)	
79	FU_PTH	Follow up serum PTH levels in the patients at follow up once between 1-6 months (in pg/ml)	

S_NO	ID	AGE	SEX	DURA_M	HEMAT_U	POLY_U	R_STONES	B_PAINS	FRACTURE	P_ABD	CONST_N	DEPRES_N	ANXIETY	NO_SYMP
1	1308840	56	2	23	2	1	2	1	2	1	1	2	1	2
2	1309983	61	2	17	2	1	2	1	2	1	1	1	1	2
3	1313272	75	1	27	2	1	2	1	1	1	1	1	1	2
4	1302328	66	2	34	2	2	2	1	2	1	2	1	1	2
5	1308662	60	2	56	2	1	2	1	2	1	1	2	1	2
6	1206176	50	1	12	2	2	1	2	2	1	1	2	1	2
7	1359934	41	2	5	2	2	1	1	2	1	1	2	2	2
8	1403791	55	2	13	2	2	2	1	2	1	1	2	2	2
9	1176262	71	1	56	2	1	2	1	1	1	2	2	1	2
10	1418834	63	2	38	2	2	2	1	2	1	1	2	2	2
11	1146563	46	2	34	2	1	1	1	2	1	1	1	2	2
12	1413008	58	2	32	2	1	2	2	2	1	2	2	1	2
13	1411023	58	1	7	2	1	2	1	2	1	1	2	1	2
14	1448795	70	1	34	2	2	2	1	2	1	1	1	1	2
15	1212740	68	2	56	1	2	2	1	1	2	2	1	1	2
16	1235028	32	1	19	1	1	1	1	2	2	1	1	1	2
17	1226505	65	2	12	2	1	2	1	2	1	2	2	2	2
18	1374269	66	2	11	2	2	2	1	2	2	1	2	2	2
19	1453842	62	2	24	2	2	2	1	2	2	2	1	1	2
20	1370568	64	2	32	1	1	1	1	2	1	2	2	2	2
21	1367649	37	1	25	2	2	1	2	2	1	2	2	1	2
22	1337374	57	2	27	2	2	1	2	2	1	2	2	2	2
23	1341913	58	2	0	2	2	2	1	2	2	2	2	2	1
24	1344576	52	2	0	2	2	2	2	2	2	2	2	2	1
25	1342131	29	1	21	2	2	2	1	2	2	1	1	1	2
26	976994	48	1	0	2	2	2	2	2	2	2	2	2	1
27	1347455	62	2	42	2	1	1	1	1	2	1	1	1	2
28	569434	54	2	35	2	1	2	1	2	2	1	2	2	2
29	1354822	72	2	36	2	1	2	2	2	2	1	1	1	2
30	1539426	40	2	27	2	2	2	1	2	1	1	1	1	2
31	1443656	33	2	23	2	1	1	1	1	1	1	1	1	2
32	1460594	45	1	9	2	2	2	1	2	2	2	2	2	2
33	1477598	62	1	12	1	1	2	1	2	1	2	2	2	2
34	1407110	44	2	34	2	1	2	1	2	2	2	1	1	2
35	1476891	60	2	16	2	2	2	1	2	1	2	1	1	2
36	1482015	39	2	10	2	1	2	2	2	2	2	2	1	2
37	1531731	21	1	6	2	2	2	1	2	1	1	1	1	2
38	1521237	82	2	13	2	1	1	1	2	2	2	1	1	2
39	1572178	19	1	23	2	1	1	1	2	1	2	2	2	2
40	525389	74	2	14	1	1	2	1	1	1	1	1	2	2
41	1594994	41	2	35	2	1	2	1	1	1	1	1	2	2
42	953866	35	1	0	2	2	2	2	2	2	2	2	2	1
43	231799	50	2	32	1	1	1	1	2	2	2	2	2	2
44	1620326	65	2	24	2	2	2	2	2	1	1	1	1	2

S_NO	ID	DM	HTN	CAD	CVA	SBP	DBP	HR	JAW_SW	DIS_PW	PROX_PW	MMSE	PHQ4	HB	NLR
1	1308840	1	2	2	2	110	70	68	2	5	4	28	6	9.9	10.38
2	1309983	1	1	2	2	180	90	72	2	4	3	20	9	8.4	1.76
3	1313272	1	1	2	2	140	80	61	2	5	5	21	10	14	4.15
4	1302328	2	1	2	2	170	80	78	2	5	4	26	11	9.8	3.38
5	1308662	1	1	2	2	150	90	76	2	5	4	28	3	9.6	3.74
6	1206176	2	2	2	2	130	80	67	2	5	5	30	4	13.2	0.79
7	1359934	2	2	2	2	140	80	65	2	5	5	30	0	10.4	3.01
8	1403791	2	1	2	2	160	70	84	2	4	4	28	1	14.9	2.79
9	1176262	1	2	2	2	120	80	86	2	5	5	30	5	9.6	4.73
10	1418834	1	1	2	2	120	80	69	2	3	3	24	2	11.1	1.52
11	1146563	2	2	2	2	120	70	65	2	4	4	30	12	10.9	2.33
12	1413008	1	1	2	2	140	80	78	2	5	5	30	5	9.5	3.83
13	1411023	1	1	2	2	160	80	58	2	4	3	30	4	10.5	6.75
14	1448795	2	2	2	2	120	80	76	2	4	4	30	9	9.4	6.61
15	1212740	1	1	1	1	180	100	86	2	3	4	20	10	10.8	21.55
16	1235028	2	1	2	2	150	80	71	2	5	4	30	11	9.4	6.61
17	1226505	1	1	2	2	140	90	76	2	4	3	24	0	9	1.53
18	1374269	1	2	2	2	120	80	65	2	5	5	30	0	8	2.32
19	1453842	2	2	2	2	110	70	68	2	4	4	28	3	8.9	11.22
20	1370568	1	2	2	2	110	70	74	2	3	4	22	0	7.2	10.99
21	1367649	2	2	2	2	120	76	62	2	5	5	30	3	11	1.88
22	1337374	1	1	2	2	160	80	70	2	4	3	26	1	8	3.50
23	1341913	2	2	2	1	120	70	77	2	3	2	30	2	8.4	4.44
24	1344576	2	2	2	2	110	80	67	2	5	5	30	0	11.2	2.29
25	1342131	2	2	2	2	100	60	64	2	5	5	30	12	8.2	1.97
26	976994	2	2	2	2	120	70	78	2	5	5	30	0	11	1.16
27	1347455	1	1	2	2	160	100	80	2	4	3	20	12	8.2	2.30
28	569434	2	1	1	2	140	90	84	2	4	3	18	0	8.7	1.90
29	1354822	2	1	2	2	190	90	81	2	4	3	19	11	9.1	3.51
30	1539426	2	1	2	2	160	100	84	2	4	4	27	10	9.5	1.41
31	1443656	2	2	2	2	110	70	78	2	5	5	30	9	12.8	3.00
32	1460594	2	2	2	2	120	70	79	2	5	5	30	1	8.4	3.08
33	1477598	1	1	1	2	110	70	89	2	4	5	24	4	13.4	3.94
34	1407110	1	1	1	2	180	90	86	2	4	4	30	5	9.8	1.87
35	1476891	1	1	2	2	160	90	84	2	3	4	20	9	12.7	5.30
36	1482015	2	2	2	2	110	70	76	2	5	5	30	5	11.2	2.64
37	1531731	2	2	2	2	110	70	76	2	5	5	30	2	10.4	1.44
38	1521237	1	1	1	1	160	90	88	2	3	3	18	4	8.3	1.13
39	1572178	1	2	2	2	110	70	54	2	5	5	30	0	11.4	3.58
40	525389	1	1	1	1	160	100	67	2	4	3	18	0	8.6	4.17
41	1594994	1	1	2	2	160	80	72	2	4	3	20	3	9.8	4.09
42	953866	2	2	2	2	110	70	66	2	5	5	30	0	12.9	9.86
43	231799	1	1	2	1	140	90	64	2	4	3	26	2	9.1	5.36
44	1620326	1	1	2	2	140	80	75	2	4	3	22	10	9.8	16.73

S_NO	ID	PLT	ALP	ALB	CA	C_CA	PTH	VITD	PHOS	UA	AMYLASE	LIPASE	U_CA	EF	FS
1	1308840	525	157	3.03	11.6	12.376	1117	32	1.46	6.3	980	1008	242	60	30
2	1309983	217	1201	4.09	10.2	10.2	2800	21	2	-	-	-	167	45	23
3	1313272	169	76	3.91	11.1	11.172	30.54	23.11	2	7.8	-	-	226	60	30
4	1302328	140	107	3.53	10.6	10.976	174	59.76	1.8	4.8	-	-	156	60	30
5	1308662	358	94	4.27	10.3	10.3	76	30	2.3	-	-	-	189	55	28
6	1206176	193	174	4.26	11.5	11.5	690	32	1.6	-	-	-	220	45	20
7	1359934	240	157	3.69	9.352	9.6	281.3	23.4	1.72	5.5	532	784	352	60	30
8	1403791	348	82	4.48	9.6	9.6	111.8	23	1.4	5.2	57	52	279	60	30
9	1176262	140	107	3.4	12.12	12.6	44.2	66.9	3.8	6.3	1875	2030	232	60	30
10	1418834	184	107	3.5	10.3	10.7	1843	32	1.46	6.8	346	493	226	60	30
11	1146563	327	127	4.16	12.3	12.3	240.7	30.6	3	5.8	-	-	295	55	28
12	1413008	504	145	2.91	11.528	12.4	245.4	33	2.4	5.2	144	326	223	60	30
13	1411023	372	150	3.63	17.2	17.496	1682	9.91	2.8	8	160	177	419	60	30
14	1448795	459	107	2.07	10.3	11.844	81.9	18.79	2.15	7	71	20	178	60	30
15	1212740	550	75	2.36	10.1	11.412	276.7	13.8	3.83	5.6	-	-	182	-	-
16	1235028	459	100	2.2	11.3	12.74	210	20	2	7	70	25	252	-	-
17	1226505	160	57	2.2	10.3	11.74	93	10	2	7	107	68	220	60	30
18	1374269	273	100	3.2	12.8	13.44	328.9	20	2.4	7.4	-	-	287	60	30
19	1453842	362	150	3.4	12.9	13.38	944	22	1.8	6.8	-	-	282	-	-
20	1370568	140	245	2.7	11	12.04	49.8	27.6	1.19	3.9	-	-	292	60	30
21	1367649	332	84	4	13.6	13.6	710	24	2.4	6.3	-	-	272.6	-	-
22	1337374	455	50	2.8	11.5	12.46	259.5	12	1.6	7.8	38	42	292	60	30
23	1341913	228	84	3.2	10.24	10.88	87	12	2.4	4.8	40	46	220	-	-
24	1344576	228	46	4	11.4	11.4	337.2	18	2.7	4.3	-	-	248	-	-
25	1342131	284	54	4.2	12.6	12.6	600.8	22	2.9	4.8	-	-	290	-	-
26	976994	165	214	3.8	11.5	11.66	246	53	1.7	7.2	-	-	224	50	30
27	1347455	444	214	2.8	11.7	12.66	238.6	38	1.8	4.7	-	-	297	-	-
28	569434	201	85	4.8	10.7	10.7	124	32.8	3.24	9	-	-	242	-	-
29	1354822	238	66	3.2	12.3	12.94	698.2	26	2.3	4.9	-	-	198	60	30
30	1539426	468	244	4.5	12.03	12.03	97	17.24	1.7	7	99	70	248	60	30
31	1443656	178	123	3.96	11.1	11.132	206.5	18	2.8	5.4	-	-	287	-	-
32	1460594	183	1526	4.5	12.4	12.4	2986	3.3	1.6	7.8	-	-	197	60	30
33	1477598	359	125	4.4	10.6	10.6	33.4	31.5	4.29	-	-	-	237	-	-
34	1407110	305	211	3.7	10.7	10.94	464.7	23	2.3	7.8	-	-	142	45	20
35	1476891	75	104	3.8	10.9	11.06	199.1	39.5	2.3	5.2	1589	4787	142	60	30
36	1482015	202	73	4.8	11.4	11.4	135.8	27	3.4	5.4	-	-	201	-	-
37	1531731	272	110	3.5	11.6	12	53	9.2	2.6	4.2	-	-	142	-	-
38	1521237	320	133	2.6	10.4	11.52	177.3	3.3	2.8	7.8	-	-	148	-	-
39	1572178	300	176	2.86	13.4	14.312	86.06	31.76	1.7	9.6	2864	1782	248	-	-
40	525389	82	183	2.3	11.27	12.63	96.64	23	1.37	7.3	182	267	217	-	-
41	1594994	99	136	2.8	10.8	11.76	362	20.8	3.6	5.8	-	-	284	30	20
42	953866	296	82	4.5	12.2	12.2	419.5	19.4	1.4	5.3	394	678	242	-	-
43	231799	232	178	3.2	12.2	12.84	2373	17	1.6	6.2	-	-	248	60	30
44	1620326	218	102	2.1	11.5	13.02	538.9	32	2.2	4.4	495	285	282	60	30

S_NO	ID	E	A	E:A	E_IVST(D)	E_LVID(D)	E_LVPW(D)	LVMI	PASP	AVC	X_RAY	USG_NECK	TC99
1	1308840	54	91	0.59	1.2	3.6	1.3	87.59	56	1	1	1	LIPA
2	1309983	67	96	0.70	0.8	5.1	1.7	149.77	57	1	1	1	ECTOPIC
3	1313272	55	65	0.85	1.5	4.7	1.5	171.55	23	2	1	1	RIPA
4	1302328	83	137	0.61	0.9	4.6	0.9	81.06	34	2	1	2	LIPA
5	1308662	67	140	0.48	1.2	4.8	1.2	128.36	32	2	1	2	2
6	1206176	70	132	0.53	0.9	4.4	1.3	98.87	12	2	2	1	RIPA
7	1359934	65	69	0.94	0.8	4.4	0.9	69.77	23	2	2	1	LIPA
8	1403791	48	76	0.63	3.3	4.5	1.3	320.27	24	2	-	1	LIPA
9	1176262	50	78	0.64	0.8	4.8	0.8	74.93	32	2	1	2	2
10	1418834	58	111	0.52	0.9	3.8	0.9	59.08	55	1	2	1	-
11	1146563	52	74	0.70	0.8	4	0.8	54.86	34	2	2	1	2
12	1413008	62	100	0.62	1.2	4.6	1.3	127.12	36	2	2	1	RIPA
13	1411023	82	42	1.95	0.9	4.9	0.9	90.24	44	1	2	1	LIPA
14	1448795	44	65	0.68	0.9	4.9	1	96.81	21	2	-	1	RIPA
15	1212740	-	-	-	-	-	-	-	-	-	2	2	-
16	1235028	-	-	-	-	-	-	-	-	-	1	-	LIPA
17	1226505	54	89	0.61	1.2	4.2	1.3	110.38	27	2	2	1	RIPA
18	1374269	45	88	0.51	1.3	2.8	1.1	57.47	22	2	2	1	LIPA
19	1453842	-	-	-	-	-	-	-	-	-	-	1	RIPA
20	1370568	65	70	0.93	0.8	4.4	0.9	69.77	24	2	1	1	RIPA
21	1367649	-	-	-	-	-	-	-	-	-	2	1	LIPA
22	1337374	58	98	0.59	0.9	3.8	0.9	59.08	32	2	2	2	RIPA
23	1341913	-	-	-	-	-	-	-	-	-	1	2	RSPA
24	1344576	-	-	-	-	-	-	-	-	-	-	1	LIPA
25	1342131	-	-	-	-	-	-	-	-	-	-	1	LIPA
26	976994	46	69	0.67	0.9	4.8	1	93.50	14	2	2	1	RIPA
27	1347455	-	-	-	-	-	-	-	-	-	-	1	LSPA
28	569434	-	-	-	-	-	-	-	-	-	-	1	2
29	1354822	56	114	0.49	1.2	3.9	1.2	92.82	33	2	2	2	LIPA
30	1539426	65	96	0.68	0.8	4.4	0.9	69.77	23	2	2	1	LIPA
31	1443656	-	-	-	-	-	-	-	-	-	2	1	2
32	1460594	95	53	1.79	0.8	4.5	1	78.12	64	1	2	1	RIPA
33	1477598	-	-	-	-	-	-	-	-	-	-	-	-
34	1407110	56	98	0.57	1.2	4.8	1	113.82	32	2	2	2	LIPA
35	1476891	56	65	0.86	0.9	3.8	1.2	73.40	21	2	2	1	-
36	1482015	-	-	-	-	-	-	-	-	-	2	1	LIPA
37	1531731	-	-	-	-	-	-	-	-	-	2	1	2
38	1521237	-	-	-	-	-	-	-	-	-	-	1	2
39	1572178	-	-	-	-	-	-	-	-	-	2	1	-
40	525389	-	-	-	-	-	-	-	-	-	-	2	-
41	1594994	48	77	0.62	1.9	2.3	2	108.99	18	2	2	1	-
42	953866	-	-	-	-	-	-	-	-	-	-	1	RIPA
43	231799	84	90	0.93	0.9	4.6	0.9	81.06	66	1	1	2	RIPA
44	1620326	49	73	0.67	1.2	4.6	1.2	119.95	48	2	2	-	-

S_NO	ID	USG_WA	PT_MODE	IVF	FUROSE	CALCITO	CINACAL	ZOLEDRO	DENOSU	HD	CA_NOR_H	CA_NOR_Z	CA_NOR_D
1	1308840	AP	2	1	1	1	1	1	2	2	9	2	-
2	1309983	NS	2	1	1	1	2	2	2	1	16	-	-
3	1313272	NS	2	1	1	1	1	2	2	2	9	-	-
4	1302328	NS	2	1	1	1	1	1	2	2	6	2	-
5	1308662	RPC	1	-	-	-	-	-	-	-	-	-	-
6	1206176	CP	2	1	1	1	1	2	2	2	4	-	-
7	1359934	AP	2	1	1	1	1	2	2	2	5	-	-
8	1403791	RPC	1	-	-	-	-	-	-	-	-	-	-
9	1176262	RC	1	-	-	-	-	-	-	-	-	-	-
10	1418834	AP	2	1	1	1	2	2	2	2	2	-	-
11	1146563	RC	2	1	1	1	1	1	2	2	6	2	-
12	1413008	AP	2	1	1	1	1	1	2	2	6	2	-
13	1411023	AP	2	1	1	1	2	2	2	2	4	-	-
14	1448795	NS	1	-	-	-	-	-	-	-	-	-	-
15	1212740	NS	1	-	-	-	-	-	-	-	-	-	-
16	1235028	RC	1	-	-	-	-	-	-	-	-	-	-
17	1226505	NS	2	1	1	1	1	1	2	2	7	2	-
18	1374269	NS	2	1	1	1	1	2	2	2	4	-	-
19	1453842	-	1	-	-	-	-	-	-	-	-	-	-
20	1370568	RC	2	1	1	1	1	2	2	2	6	-	-
21	1367649	NS	2	1	1	1	1	2	2	2	4	-	-
22	1337374	RC	2	1	1	1	1	1	2	2	10	3	-
23	1341913	NS	1	-	-	-	-	-	-	-	-	-	-
24	1344576	NS	1	-	-	-	-	-	-	-	-	-	-
25	1342131	-	1	-	-	-	-	-	-	-	-	-	-
26	976994	NS	2	1	1	1	1	1	1	2	15	7	3
27	1347455	NS	1	-	-	-	-	-	-	-	-	-	-
28	569434	NS	1	-	-	-	-	-	-	-	-	-	-
29	1354822	NS	2	1	1	1	1	1	2	2	6	4	-
30	1539426	NS	2	1	1	1	1	2	1	2	7	-	3
31	1443656	NS	2	1	1	1	1	1	2	2	8	3	-
32	1460594	NS	2	1	1	1	1	1	2	2	12	4	-
33	1477598	-	1	-	-	-	-	-	-	-	-	-	-
34	1407110	-	2	1	1	1	2	2	2	2	3	-	-
35	1476891	NS	2	1	1	1	1	1	2	2	12	4	-
36	1482015	-	2	1	1	1	1	1	2	2	8	3	-
37	1531731	NS	2	1	1	1	2	2	2	2	4	-	-
38	1521237	RC	1	-	-	-	-	-	-	-	-	-	-
39	1572178	RC	2	1	1	1	2	1	2	2	7	4	-
40	525389	AP	1	-	-	-	-	-	-	-	-	-	-
41	1594994	-	2	1	1	1	1	1	2	2	13	4	-
42	953866	AP	1	-	-	-	-	-	-	-	-	-	-
43	231799	RC	2	1	1	1	1	1	2	2	12	4	-
44	1620326	AP	2	1	1	1	2	1	2	2	6	3	-

S_NO	ID	SURGERY	HBS	HBSCA	HIS_SZ_A	HIS_SZ_B	HIS_SZ_C	HIS_WT	HIS_S/O	OUTCOME	FU_CA	FU_CCA	FU_PTH
1	1308840	1	2	-	3.5	1.5	0.8	7	PA	FU	8.9	9.14	11
2	1309983	1	1	4.4	2.4	1	0.8	6	PA	EXP	-	-	-
3	1313272	1	2	-	1.5	1	0.5	4	PA	FU	8.8	9.04	16.5
4	1302328	1	2	-	5.4	1	0.4	6	PA	FU	8.4	8.64	2.8
5	1308662	2	-	-	-	-	-	-	-	FU	8.6	8.84	3.7
6	1206176	1	2	-	1.3	0.7	0.5	2	PA	FU	9	9.24	10.7
7	1359934	1	2	-	1.8	1.3	1	5	PA	FU	8.8	9.04	14
8	1403791	2	-	-	-	-	-	-	-	FU	9.3	9.54	17
9	1176262	2	-	-	-	-	-	-	-	LTFU	-	-	-
10	1418834	1	2	-	1.5	1	0.5	4	PA	FU	8.8	9.04	27
11	1146563	2	-	-	-	-	-	-	-	FU	9.3	9.54	16.7
12	1413008	1	2	-	2	1	0.8	10	PA	FU	9	9.24	32
13	1411023	1	1	5.2	2.2	2	1.2	4	PA	FU	9	9.24	28
14	1448795	2	-	-	-	-	-	-	-	FU	9	9.24	15
15	1212740	2	-	-	-	-	-	-	-	EXP	-	-	-
16	1235028	2	-	-	-	-	-	-	-	LTFU	-	-	-
17	1226505	2	-	-	-	-	-	-	-	FU	8.2	8.44	12
18	1374269	1	1	4.2	1	0.7	0.3	6	PA	FU	8.2	8.44	8.9
19	1453842	2	-	-	-	-	-	-	-	FU	8.6	8.84	18
20	1370568	1	2	-	1.4	0.8	0.2	4	PA	FU	8.4	8.64	16
21	1367649	1	2	-	1.3	0.7	0.5	4	PA	FU	8.6	8.84	17
22	1337374	2	-	-	-	-	-	-	-	FU	9.2	9.44	18.9
23	1341913	2	-	-	-	-	-	-	-	FU	8.2	8.44	15.4
24	1344576	2	-	-	-	-	-	-	-	FU	9.4	9.64	7.8
25	1342131	2	-	-	-	-	-	-	-	FU	8.7	8.94	4.6
26	976994	2	-	-	-	-	-	-	-	FU	9.3	9.54	6.3
27	1347455	2	-	-	-	-	-	-	-	FU	9.7	9.94	6.4
28	569434	2	-	-	-	-	-	-	-	FU	9.7	9.94	111
29	1354822	1	2	-	1.3	1	0.5	9	PA	FU	9.2	9.44	22
30	1539426	2	-	-	-	-	-	-	-	FU	9.9	10.14	38
31	1443656	1	2	-	2.5	1.5	1	10	PCA	FU	8.8	9.04	28
32	1460594	1	2	-	0.8	0.5	0.3	3	PA	FU	9.9	10.14	36
33	1477598	2	-	-	-	-	-	-	-	FU	8.4	8.64	80
34	1407110	1	2	-	3.4	2.4	2.1	17	PA	FU	9	9.24	28
35	1476891	2	-	-	-	-	-	-	-	LTFU	-	-	-
36	1482015	1	2	-	3.4	2.1	0.8	9	PA	FU	8.8	9.04	38
37	1531731	1	2	-	5.8	3.4	1.9	24	INC	FU	8.8	9.04	32
38	1521237	2	-	-	-	-	-	-	-	FU	9	9.24	36
39	1572178	1	2	-	3.1	2.8	0.4	16	PA	FU	9.8	10.04	60
40	525389	2	-	-	-	-	-	-	-	EXP	-	-	-
41	1594994	1	2	-	2.6	1.8	0.7	7	PCA	FU	8.7	8.94	22
42	953866	2	-	-	-	-	-	-	-	FU	8.6	8.84	26.17
43	231799	1	2	-	1.4	0.9	0.3	6	PA	FU	8.5	8.74	16
44	1620326	1	2	-	3.4	2.1	1.1	10	PA	FU	8.2	8.44	12

S_NO	ID	AGE	SEX	DURA_M	HEMAT_U	POLY_U	R_STONES	B_PAINS	FRACTURE	P_ABD	CONST_N	DEPRES_N	ANXIETY	NO_SYMP
45	1613637	62	1	8	2	1	2	1	2	2	2	2	2	2
46	1562314	63	2	0	2	2	2	1	2	2	2	2	2	1
47	1538768	47	1	16	2	2	2	2	2	1	2	2	2	2
48	1476816	57	2	27	2	2	2	1	2	1	1	1	1	2
49	482210	29	1	34	1	1	1	1	2	2	1	1	1	2
50	1541668	68	2	42	2	1	2	1	2	1	1	2	2	2
51	1586329	72	2	53	2	1	1	1	2	1	2	2	2	2
52	1519233	39	2	22	2	2	2	1	2	2	1	2	2	2
53	1537090	45	2	21	2	2	2	1	1	2	1	1	2	2
54	298909	56	2	11	2	2	2	1	1	2	2	2	1	2
55	1641735	47	2	32	2	2	2	2	2	2	2	2	1	1
56	1396524	40	2	5	2	2	2	1	2	1	1	1	1	2
57	1224019	72	1	37	1	1	1	1	2	1	2	1	2	2
58	1574412	77	1	56	1	1	2	1	2	1	1	2	2	2
59	1570542	40	1	13	2	2	2	1	2	1	1	1	1	2
60	1576517	69	2	45	2	1	2	1	2	1	2	2	2	2
61	1097702	72	2	13	2	2	2	1	2	2	1	1	2	2
62	1414406	54	2	23	1	1	2	1	1	1	1	1	1	2
63	1597482	62	2	34	2	1	2	1	2	2	2	1	1	2
64	1600364	37	1	78	2	2	2	2	2	1	1	1	1	2
65	1600098	33	2	11	2	2	2	1	1	2	2	2	1	2
66	1587498	66	2	12	2	2	2	1	2	1	1	1	1	2
67	1599812	54	1	23	1	1	1	2	2	1	2	2	1	2
68	1598333	53	1	0	2	2	2	1	2	2	2	2	2	1
69	1606064	42	2	0	2	2	2	1	2	2	2	2	2	1
70	1612623	75	2	57	2	2	2	1	2	1	2	1	2	2
71	1613178	48	1	14	2	2	2	2	2	1	1	2	1	2
72	1554781	38	1	12	1	1	1	2	2	2	1	2	2	2
73	1619537	70	2	7	2	2	2	1	2	1	1	1	1	2
74	1167560	62	2	23	1	1	1	2	2	2	2	2	2	2
75	87549	39	1	21	2	2	2	2	2	1	2	2	1	2
76	1562919	30	1	15	2	2	2	2	2	1	1	2	1	2
77	1309680	70	1	17	2	2	2	2	2	2	1	1	2	2
78	700297	55	2	0	2	2	2	2	2	2	2	2	2	1
79	1633385	40	1	22	2	2	2	2	2	1	2	2	2	2
80	1640147	62	1	0	2	2	2	2	2	2	2	2	2	1
81	1465961	30	2	34	1	1	2	2	2	2	2	2	2	2
82	1647372	45	1	0	2	2	2	2	2	2	2	2	2	1
83	187653	49	2	19	1	1	1	1	2	2	1	2	2	2
84	1243133	60	2	12	2	1	2	1	2	2	2	2	2	2
85	1244537	35	1	4	2	2	2	2	2	1	1	1	1	2
86	1251463	71	1	5	1	1	2	1	2	2	2	2	2	2
87	1255834	53	2	8	2	2	2	1	2	2	1	2	2	1
88	222540	46	2	14	2	2	2	1	1	2	2	2	2	2

S_NO	ID	DM	HTN	CAD	CVA	SBP	DBP	HR	JAW_SW	DIS_PW	PROX_PW	MMSE	PHQ4	HB	NLR
45	1613637	1	1	2	1	150	80	62	2	4	4	20	1	11.4	23.46
46	1562314	2	1	2	2	120	80	78	2	4	4	28	0	12.9	2.23
47	1538768	2	2	2	2	100	60	84	2	5	5	30	0	12	8.19
48	1476816	1	1	1	2	120	88	88	2	4	4	30	11	13.8	1.90
49	482210	2	1	2	2	160	90	78	2	5	5	30	12	9.7	3.83
50	1541668	1	2	2	2	110	70	87	2	4	4	24	1	10.6	3.17
51	1586329	2	1	2	2	140	90	68	2	5	5	30	2	7.9	5.53
52	1519233	2	2	2	2	110	70	72	2	5	5	30	3	8.5	1.15
53	1537090	1	1	2	1	160	100	67	2	3	2	24	7	8.2	2.44
54	298909	2	1	2	2	150	90	87	2	4	3	24	4	7.8	5.32
55	1641735	1	1	2	2	140	90	76	2	5	4	22	5	8.5	1.59
56	1396524	2	2	2	2	140	80	62	1	4	3	24	12	9.9	7.59
57	1224019	1	1	2	1	140	80	88	2	4	3	24	5	11.8	2.27
58	1574412	1	1	1	1	150	110	62	1	3	3	18	0	8.1	9.25
59	1570542	2	2	2	1	120	70	64	2	5	5	30	11	10.7	2.54
60	1576517	1	1	2	2	130	80	78	2	5	4	28	0	8.7	3.30
61	1097702	1	1	2	2	170	90	82	2	4	3	20	4	11.2	2.09
62	1414406	1	1	2	2	130	80	64	1	4	4	28	10	7.5	5.41
63	1597482	1	1	2	2	110	60	89	2	4	4	26	9	8.5	2.47
64	1600364	2	2	2	2	130	80	61	2	5	5	30	8	13.5	4.67
65	1600098	2	2	2	2	110	60	89	2	5	5	30	3	7.6	4.36
66	1587498	2	1	2	2	130	80	60	2	4	4	28	9	9.7	6.47
67	1599812	1	1	2	2	110	70	67	2	5	5	30	3	8.5	5.64
68	1598333	2	2	2	2	110	70	78	2	5	5	30	2	11.9	0.93
69	1606064	2	2	2	2	120	70	67	2	5	5	30	1	8.3	2.67
70	1612623	1	1	2	2	140	90	72	2	4	3	22	4	8.3	2.67
71	1613178	1	1	2	2	130	90	64	2	5	5	20	5	8.3	2.67
72	1554781	2	2	2	2	120	60	64	2	5	5	30	8	15.3	2.09
73	1619537	1	1	2	2	170	90	68	2	4	5	16	10	8.3	2.67
74	1167560	1	1	1	2	130	70	70	2	4	3	24	0	11.3	6.22
75	87549	2	2	2	2	110	70	55	2	5	5	30	5	10	5.15
76	1562919	1	2	2	2	120	80	70	2	5	5	30	7	13	2.09
77	1309680	1	1	1	1	150	80	82	2	4	4	22	6	11.4	2.34
78	700297	1	2	2	2	120	70	82	2	5	5	30	0	12	1.54
79	1633385	2	2	2	2	130	80	61	2	5	5	30	0	15	1.60
80	1640147	1	2	2	2	120	70	60	2	5	5	30	1	12.7	3.69
81	1465961	2	2	2	2	110	60	78	2	5	5	30	2	5.6	3.30
82	1647372	2	2	2	2	100	60	61	2	5	4	28	4	10	4.59
83	187653	1	2	2	2	130	70	78	2	5	5	26	0	11.8	4.17
84	1243133	1	2	2	2	120	60	59	1	4	3	22	0	9.4	1.78
85	1244537	2	2	2	2	110	70	63	1	5	5	30	11	15	1.60
86	1251463	2	2	2	2	120	70	65	2	5	4	24	0	12.4	3.14
87	1255834	2	2	2	2	110	80	55	2	5	5	30	0	9.7	6.47
88	222540	2	2	2	2	120	70	58	2	5	5	30	2	10	4.59

S_NO	ID	PLT	ALP	ALB	CA	C_CA	PTH	VITD	PHOS	UA	AMYLASE	LIPASE	U_CA	EF	FS
45	1613637	202	89	2.2	17.7	19.14	916.7	21	1.6	6.3	-	-	407	-	-
46	1562314	195	68	4.2	11.3	11.3	1082	24	1.7	5.3	-	-	242	60	30
47	1538768	191	158	2.29	10.7	12.068	218.7	24	2.4	3.5	1628	965	213.6	60	30
48	1476816	221	277	4.3	9.5	9.5	126.8	49	2.4	3.9	936	482	209.4	60	30
49	482210	195	225	3.4	10.8	11.28	1442	33	4.3	7.3	-	-	249	-	-
50	1541668	436	207	3	11.5	12.3	92.9	13.7	1.6	4.8	689	938	189	60	30
51	1586329	90	123	3.8	12.6	12.76	186	12.3	2.04	6.5	-	-	201	60	30
52	1519233	159	178	3.8	11.8	11.96	165.2	26.5	2.8	5.6	-	-	247	-	-
53	1537090	344	147	2.27	11.15	12.534	93	27	1.98	6.9	-	-	178	-	-
54	298909	100	249	3.65	9.3	9.58	2745	18.6	4.3	7.4	-	-	98	50	22
55	1641735	159	1600	3.8	12.1	12.26	892.2	26.5	2.8	5.6	-	-	247	-	-
56	1396524	110	680	2.6	14.3	15.42	3009	211	1.6	-	195	211	245	60	30
57	1224019	224	78	4.2	11.2	11.2	54.4	13.8	2.4	4.8	-	-	189	60	30
58	1574412	268	73	3.4	14.9	15.38	988	28	2.1	9.6	25	103	321	60	30
59	1570542	455	193	2	13.15	14.75	119.4	8.6	2.4	-	2661	3621	301	60	30
60	1576517	252	94	4	11.8	11.8	80	41	1.8	7.5	-	-	393	60	30
61	1097702	171	130	4.3	11.5	11.5	206	30	2.7	5.6	-	-	241	60	30
62	1414406	255	138	3.2	14.5	15.14	164.8	36	1.8	5.2	1872	3482	292	60	30
63	1597482	208	731	3.72	9.9	10.124	1710	56	2.2	-	-	-	98	26	13
64	1600364	80	342	3.2	12.02	12.66	1024	13	2.1	4.5	1879	2345	213	-	-
65	1600098	90	276	3.8	9.61	9.77	69.2	11	2.1	5.3	-	-	113	-	-
66	1587498	222	154	3.7	12.2	12.44	72	11.58	3.4	4.9	555	592	228	60	30
67	1599812	392	936	1.8	12.9	14.66	231.8	8.29	2.8	5.6	1078	689	253	60	30
68	1598333	309	133	4.15	10.1	10.1	144	24	-	-	-	-	198	-	-
69	1606064	150	65	4.12	11.1	11.1	280	35	2.3	-	-	-	156	-	-
70	1612623	150	65	4.12	11.1	11.1	75	12	-	-	-	-	245	60	30
71	1613178	150	65	4.12	11.1	11.1	643	34	-	-	-	-	361	46	23
72	1554781	168	117	4.07	11.4	11.4	91.4	11.38	2.2	5.4	79	98	242	46	23
73	1619537	150	65	4.12	14	14	251	35	2.3	6.4	145	367	259	60	30
74	1167560	343	113	4.11	11	11	229.6	22.13	3.6	5.9	-	-	267	60	30
75	87549	434	134	3.8	15.7	15.86	678	21	2.7	4.5	1236	789	332	60	30
76	1562919	168	117	4.07	11	11	113.5	12	2.1	-	-	-	249	-	-
77	1309680	200	70	4.34	10.6	10.6	152	13	1.8	6.5	-	-	189	20	20
78	700297	112	130	4.1	11.7	11.7	223	34.2	3.4	5.5	-	-	139	-	-
79	1633385	229	166	4.88	14.4	14.4	136	21	2.9	5.6	-	-	245	60	30
80	1640147	309	123	4.4	12.3	12.3	234	16	3.7	4.8	-	-	178	60	30
81	1465961	244	114	2.88	10.2	11.096	1275	23	4	3.5	-	-	130	60	30
82	1647372	454	109	3.8	13.6	13.76	169	5	2.3	4.5	-	-	276	-	-
83	187653	158	129	4.2	10.5	10.5	122.5	41.93	2.4	5.2	-	-	207.4	60	30
84	1243133	172	241	3.4	15.8	16.28	1037	24	2.8	7.4	-	-	329	50	22
85	1244537	229	166	4.88	14.7	14.7	527.9	21	2.9	5.6	1345	1097	335	60	30
86	1251463	135	172	4.6	14	14	377.5	18.7	2	6.3	78	14	299	60	30
87	1255834	222	154	3.7	12.2	12.44	72	11.58	3.4	4.9	555	592	228	-	-
88	222540	454	109	3.8	13.6	13.76	169	15.7	2.3	4.5	-	-	335	60	30

S_NO	ID	E	A	E:A	E_IVST(D)	E_LVID(D)	E_LVPW(D)	LVMI	PASP	AVC	X_RAY	USG_NECK	TC99
45	1613637	-	-	-	1	4.2	0.8	69.62	49	2	2	1	LIPA
46	1562314	74	104	0.71	0.9	4.6	0.9	81.06	53	1	2	-	LIPA
47	1538768	88	104	0.85	0.9	3.2	0.8	41.43	21	2	1	1	-
48	1476816	77	89	0.87	1.2	3.3	0.8	54.98	14	2	2	-	RIPA
49	482210	-	-	-	-	-	-	-	-	-	-	1	2
50	1541668	88	120	0.73	1.1	3.6	0.7	54.15	32	2	2	1	LIPA
51	1586329	74	98	0.76	1.2	3.3	0.8	54.98	24	2	2	1	2
52	1519233	-	-	-	-	-	-	-	-	-	2	1	2
53	1537090	-	-	-	-	-	-	-	-	-	-	1	-
54	298909	88	160	0.55	1.3	3.1	1.4	80.06	49	1	1	1	RSPA
55	1641735	-	-	-	-	-	-	-	-	-	2	1	RIPA
56	1396524	76	65	1.17	0.7	4.8	0.9	74.93	58	1	1	1	LIPA
57	1224019	89	100	0.89	0.9	4.6	0.9	81.06	44	2	2	1	-
58	1574412	84	56	1.5	1.2	4.6	1.2	119.95	42	2	2	1	LIPA
59	1570542	84	67	1.25	0.8	3.2	1.1	48.64	34	2	2	1	LIPA
60	1576517	63	76	0.83	0.9	4.4	1	80.86	25	2	-	1	LIPA
61	1097702	80	50	1.6	1	4.1	0.8	66.90	33	2	-	1	LIPA
62	1414406	88	97	0.91	1.2	3.2	0.9	56.45	11	2	2	2	LIPA
63	1597482	137	105	1.30	0.6	5.4	1	92.14	49	1	2	1	RIPA
64	1600364	-	-	-	-	-	-	-	-	-	1	1	RIPA
65	1600098	-	-	-	-	-	-	-	-	-	1	1	LIPA
66	1587498	67	84	0.80	1.2	4.6	1.2	119.95	25	2	2	1	ECTOPIC
67	1599812	95	110	0.86	0.9	4.6	0.9	81.06	14	2	2	2	LSPA
68	1598333	-	-	-	-	-	-	-	-	-	-	1	2
69	1606064	-	-	-	-	-	-	-	-	-	-	1	RIPA
70	1612623	88	97	0.91	1.2	3.2	0.9	56.45	21	2	1	1	RIPA
71	1613178	112	156	0.72	1	4.8	1.1	106.85	25	2	2	1	LIPA
72	1554781	112	156	0.72	1	4.8	1.1	106.85	22	2	2	2	2
73	1619537	102	73	1.40	0.8	4.2	0.9	64.51	26	2	1	1	LIPA
74	1167560	65	80	0.81	0.8	4.6	1	81.06	22	2	1	1	RIPA
75	87549	80	50	1.60	1	4.1	0.8	66.90	18	2	2	2	RIPA
76	1562919	-	-	-	-	-	-	-	-	-	1	1	RIPA
77	1309680	108	78	1.38	1.2	4.2	1	91.81	33	2	2	1	ECTOPIC
78	700297	-	-	-	-	-	-	-	-	-	-	1	LIPA
79	1633385	65	87	0.75	0.9	4.2	1	74.90	32	2	2	1	LIPA
80	1640147	88	97	0.91	1.2	3.2	0.9	56.45	12	2	2	-	RIPA
81	1465961	80	97	0.82	1	4.1	0.8	66.90	23	1	2	2	RIPA
82	1647372	-	-	-	-	-	-	-	-	-	1	1	LIPA
83	187653	76	98	0.78	1.2	4.6	1.2	119.95	28	2	2	1	LIPA
84	1243133	98	109	0.90	1.3	4.2	0.9	91.81	43	1	2	1	RIPA
85	1244537	82	67	1.22	0.9	4.9	1	96.81	22	2	2	1	RIPA
86	1251463	117	108	1.08	0.9	4.8	0.7	74.93	9	2	2	1	LIPA
87	1255834	-	-	-	-	-	-	-	-	-	-	1	LIPA
88	222540	82	61	1.34	0.9	4.9	1	96.81	16	2	2	1	RIPA

S_NO	ID	USG_WA	PT_MODE	IVF	FUROSE	CALCITO	CINACAL	ZOLEDRO	DENOSU	HD	CA_NOR_H	CA_NOR_Z	CA_NOR_D
45	1613637	NS	2	1	1	1	2	2	2	2	6	-	-
46	1562314	-	2	1	1	1	1	1	2	2	8	4	-
47	1538768	AP	2	1	1	1	1	1	2	2	10	6	-
48	1476816	NS	2	1	1	1	1	1	2	2	8	4	-
49	482210	NS	1	-	-	-	-	-	-	-	-	-	-
50	1541668	AP	2	1	1	1	2	2	2	2	8	-	-
51	1586329	RC	2	1	1	1	1	1	2	2	13	2	-
52	1519233	-	2	1	1	1	2	2	2	2	5	-	-
53	1537090	NS	1	-	-	-	-	-	-	-	-	-	-
54	298909	NS	2	1	1	1	1	1	2	2	14	6	-
55	1641735	-	2	1	1	1	1	1	2	2	16	4	-
56	1396524	RPC	2	1	1	1	2	2	2	2	10	-	-
57	1224019	-	2	1	1	1	1	1	2	2	7	3	-
58	1574412	-	2	1	1	1	1	1	2	2	12	4	-
59	1570542	AP	2	1	1	1	1	2	2	2	5	-	-
60	1576517	-	1	-	-	-	-	-	-	-	-	-	-
61	1097702	-	1	-	-	-	-	-	-	-	-	-	-
62	1414406	AP	2	1	1	1	1	1	1	2	10	7	4
63	1597482	RPC	2	2	1	2	2	2	2	1	0	-	-
64	1600364	AP	2	2	2	2	1	2	2	2	14	-	-
65	1600098	RC	2	1	1	1	1	1	2	2	9	2	-
66	1587498	NS	2	1	1	1	1	1	2	2	7	4	-
67	1599812	AP	2	1	1	1	2	2	2	2	7	-	-
68	1598333	-	1	-	-	-	-	-	-	-	-	-	-
69	1606064	-	1	-	-	-	-	-	-	-	-	-	-
70	1612623	CP	2	1	1	1	1	2	2	2	12	-	-
71	1613178	AP	2	2	2	2	1	2	1	2	12	-	4
72	1554781	AP	2	1	2	1	1	2	2	2	13	-	-
73	1619537	CP	2	1	2	1	1	1	2	2	7	4	-
74	1167560	RC	2	1	1	1	1	1	2	2	4	2	-
75	87549	AP	2	1	1	1	2	2	2	2	5	-	-
76	1562919	AP	2	1	1	1	1	1	2	2	12	4	-
77	1309680	NS	2	2	1	2	2	2	2	2	6	-	-
78	700297	NS	1	-	-	-	-	-	-	-	-	-	-
79	1633385	-	2	1	1	1	1	1	2	2	7	2	-
80	1640147	-	2	1	1	1	1	1	1	1	1	-	-
81	1465961	RPC	2	1	1	1	2	2	2	1	10	-	-
82	1647372	-	1	-	-	-	-	-	-	-	-	-	-
83	187653	RC	2	1	1	1	1	1	2	2	12	4	-
84	1243133	RPC	2	1	1	2	1	2	1	2	14	-	4
85	1244537	AP	2	2	2	2	1	2	2	2	10	-	-
86	1251463	NS	2	1	1	2	2	2	2	2	6	-	-
87	1255834	NS	1	-	-	-	-	-	-	-	-	-	-
88	222540	NS	2	1	1	2	2	2	2	2	8	-	-

S_NO	ID	SURGERY	HBS	HBSCA	HIS_SZ_A	HIS_SZ_B	HIS_SZ_C	HIS_WT	HIS_S/O	OUTCOME	FU_CA	FU_CCA	FU_PTH
45	1613637	1	2	-	2.1	1.9	0.3	9	PA	FU	8.6	8.84	30
46	1562314	2	-	-	-	-	-	-	-	FU	9.4	9.64	82
47	1538768	1	2	-	1.7	0.9	0.4	9	PA	FU	10.2	10.44	24
48	1476816	1	2	-	2.9	1.8	0.6	13	PA	FU	8.4	8.64	22
49	482210	2	-	-	-	-	-	-	-	LTFU	-	-	-
50	1541668	1	2	-	7.8	4.8	3.2	29	PCA	FU	8.6	8.84	19.7
51	1586329	1	2	-	4.2	2.9	1.2	16	PCA	FU	8.4	8.64	19
52	1519233	1	2	-	2.1	0.8	0.4	12	INC	FU	10.4	10.64	9.9
53	1537090	2	-	-	-	-	-	-	-	LTFU	-	-	-
54	298909	1	2	-	1.5	1	0.5	3	PA	FU	7.3	7.54	24
55	1641735	2	-	-	-	-	-	-	-	FU	8.2	8.44	12
56	1396524	1	1	5.3	2.1	1.2	0.4	1.8	PA	FU	9.1	9.34	8.7
57	1224019	2	-	-	-	-	-	-	-	FU	9.7	9.94	11
58	1574412	1	1	6.2	2.2	1.8	1	9	PCA	FU	8.2	8.44	7.9
59	1570542	1	2	-	2.2	1.1	0.8	5	PA	FU	8.4	8.64	14
60	1576517	2	-	-	-	-	-	-	-	FU	9.4	9.64	10.9
61	1097702	2	-	-	-	-	-	-	-	FU	8.2	8.44	17
62	1414406	1	1	5.7	2.5	2	1.7	7	PA	FU	8	8.24	16
63	1597482	1	2	-	1.5	1	1	5	PA	FU	9	9.24	12
64	1600364	1	1	4.8	4.3	2.1	1.1	7	PA	FU	8.9	9.14	11
65	1600098	1	2	-	1.9	0.7	0.3	2	PA	FU	9	9.24	12
66	1587498	2	-	-	-	-	-	-	-	FU	10.2	10.44	5.8
67	1599812	1	2	-	1.5	1	0.8	4	PA	FU	9.4	9.64	3.3
68	1598333	2	-	-	-	-	-	-	-	FU	8.4	8.64	18
69	1606064	2	-	-	-	-	-	-	-	FU	8.4	8.64	12
70	1612623	1	2	-	1.2	0.8	0.3	5	PA	FU	8.2	8.44	11
71	1613178	1	2	-	3.2	2.1	0.7	9	PA	FU	8.8	9.04	12
72	1554781	1	2	-	1.5	0.8	0.4	7.2	INC	FU	8.7	8.94	16
73	1619537	1	2	-	5.6	3.2	1.3	19	PA	FU	9.2	9.44	24
74	1167560	1	2	-	1.5	0.8	0.4	3	PA	FU	10.3	10.54	4.8
75	87549	1	2	-	0.7	0.6	0.2	4	PA	FU	8.9	9.14	21
76	1562919	1	2	-	1.2	0.9	0.6	5	PA	FU	8.8	9.04	11
77	1309680	2	-	-	-	-	-	-	-	FU	11.9	12.14	134
78	700297	2	-	-	-	-	-	-	-	FU	8.8	9.04	7.7
79	1633385	1	1	5.1	2.3	1.7	0.9	7	PA	FU	12	12.24	67
80	1640147	1	2	-	3.4	2.1	1.9	9	PA	FU	10.8	11.04	54
81	1465961	1	2	-	1.1	0.6	0.2	3	INC	FU	11.2	11.44	243
82	1647372	2	-	-	-	-	-	-	-	FU	9.8	10.04	3.2
83	187653	1	2	-	0.8	0.4	0.2	2	PA	FU	8.8	9.04	19.5
84	1243133	1	1	4.9	0.9	0.7	0.4	1.8	PA	FU	8.2	8.44	13
85	1244537	1	2	-	1.2	0.7	0.2	4	PA	FU	8.5	8.74	12
86	1251463	1	2	-	1.3	1	0.5	5	PA	FU	8.8	9.04	10.1
87	1255834	2	-	-	-	-	-	-	-	FU	8.9	9.14	12.8
88	222540	1	2	-	1.8	1	0.6	3	PA	FU	9.4	9.64	9.8

S_NO	ID	AGE	SEX	DURA_M	HEMAT_U	POLY_U	R_STONES	B_PAINS	FRACTURE	P_ABD	CONST_N	DEPRES_N	ANXIETY	NO_SYMP
89	1049624	40	2	17	2	2	2	1	2	1	1	2	2	2
90	1256792	63	2	8	2	1	2	1	2	1	1	2	2	2
91	1261392	75	1	6	2	1	2	1	2	2	1	2	2	2
92	1248039	59	1	15	2	1	1	1	1	1	1	1	1	2
93	1263047	67	2	23	2	1	2	1	2	2	1	2	2	2
94	1234540	60	2	36	1	1	2	1	2	2	1	2	2	2
95	1277431	32	2	45	2	2	2	1	1	1	1	2	1	2
96	802200	68	1	67	2	1	2	1	1	1	1	1	2	2
97	1259498	59	2	26	1	1	2	1	2	2	1	1	1	2
98	1285591	22	1	45	1	1	2	2	2	1	1	1	1	2
99	1289134	57	2	0	2	2	2	1	2	2	1	2	2	1
100	258175	32	2	42	1	1	1	1	2	2	1	1	1	2
101	1291232	40	2	0	2	1	2	1	2	1	1	2	2	1
102	292149	49	2	0	2	2	2	2	2	2	2	2	2	1
103	1294565	58	2	0	2	1	2	1	2	1	1	2	2	1
104	1291518	45	1	48	2	2	2	1	2	1	1	1	1	2
105	1237023	51	1	45	1	1	2	1	2	2	2	2	2	2
106	1359922	43	2	36	1	1	2	1	2	1	2	1	1	2
107	1367349	37	1	24	2	2	2	1	2	1	1	2	2	2
108	1382458	51	2	36	2	1	1	1	2	1	1	1	1	2
109	1381711	65	1	24	2	2	2	1	2	2	1	1	2	2
110	1392365	67	1	76	2	2	2	1	2	1	2	2	1	2
111	1393730	56	1	22	1	1	1	1	2	2	2	2	2	2
112	1357365	56	2	0	2	2	2	2	2	2	2	2	2	1
113	1397513	49	2	45	1	1	1	1	1	1	1	1	1	2
114	1405762	58	2	48	2	2	2	1	2	1	1	2	2	2
115	1413176	35	2	0	2	2	2	2	2	2	2	2	2	1
116	1413980	72	2	78	2	1	2	2	2	1	2	1	2	2
117	1426965	40	2	12	2	2	2	1	1	2	1	2	2	2
118	1428834	62	1	56	2	2	2	1	1	1	1	1	2	2
119	4348	47	2	32	2	1	2	1	1	1	1	2	2	2
120	1438958	70	1	44	1	1	1	1	2	2	1	1	2	2
121	1318401	70	2	45	2	2	2	1	2	1	1	1	2	2
122	1295112	62	2	0	2	2	2	2	2	2	2	2	2	1
123	1296110	72	2	0	2	2	2	2	2	2	2	2	2	1
124	1292650	75	2	25	1	1	1	2	2	2	2	2	2	2
125	128423	30	1	54	1	1	1	1	2	1	1	2	1	2
126	1301266	51	2	0	2	2	2	2	2	2	2	2	2	1
127	101294	25	1	42	1	1	1	1	1	1	1	2	1	2
128	985394	61	2	48	1	1	1	1	2	1	1	2	1	2

S_NO	ID	DM	HTN	CAD	CVA	SBP	DBP	HR	JAW_SW	DIS_PW	PROX_PW	MMSE	PHQ4	HB	NLR
89	1049624	2	2	2	2	120	70	62	2	5	5	30	1	13	3.35
90	1256792	1	1	2	1	110	68	67	2	1	1	20	0	12.7	3.63
91	1261392	1	2	2	2	120	78	72	2	5	5	26	0	11.7	7.69
92	1248039	2	2	2	2	130	80	71	2	5	5	28	12	7.5	3.18
93	1263047	2	1	2	2	160	80	74	2	2	1	24	0	11.9	6.37
94	1234540	1	1	2	2	150	90	76	2	5	4	26	2	13	1.57
95	1277431	2	2	2	2	140	90	80	2	5	5	30	6	10.8	7.45
96	802200	1	1	1	1	130	78	65	2	4	3	22	1	11.9	5.21
97	1259498	1	1	1	1	170	80	56	2	3	2	16	7	9.8	2.27
98	1285591	2	2	2	2	120	80	58	2	5	5	30	8	12.8	1.65
99	1289134	2	2	2	2	120	70	54	2	5	5	30	1	11.9	5.21
100	258175	2	2	2	2	110	60	78	2	5	5	30	11	10.4	4.86
101	1291232	2	2	2	2	130	90	67	2	5	4	28	0	8.1	2.92
102	292149	2	2	2	2	110	70	84	2	5	5	30	0	11.8	4.17
103	1294565	2	2	2	2	118	70	88	1	5	5	30	1	12	6.33
104	1291518	1	2	2	2	120	80	61	2	5	5	30	1	13.1	2.71
105	1237023	2	1	2	2	130	70	68	1	5	4	26	0	7.6	2.59
106	1359922	1	2	2	2	100	60	64	2	5	5	28	12	7.9	3.15
107	1367349	2	2	2	2	138	68	57	2	5	5	30	0	13.9	2.71
108	1382458	2	2	2	2	110	60	62	2	5	5	30	10	10.4	4.86
109	1381711	2	1	2	2	170	70	52	2	5	5	26	8	18.2	1.79
110	1392365	2	1	1	1	130	70	71	2	4	3	22	3	14.6	5.76
111	1393730	2	1	2	2	190	90	87	1	5	5	24	7	13.6	16.29
112	1357365	2	2	2	2	110	60	54	2	5	5	30	2	13.9	2.71
113	1397513	1	1	1	1	160	90	60	2	5	4	22	9	5.6	10.63
114	1405762	2	1	2	2	130	80	67	2	4	4	30	1	12.7	7.25
115	1413176	2	2	2	2	130	70	73	2	5	5	30	2	11.6	1.51
116	1413980	1	2	2	2	120	70	82	2	4	3	22	3	11.5	3.00
117	1426965	1	2	2	2	130	80	53	2	5	5	30	4	11.6	1.51
118	1428834	1	1	1	1	180	90	54	2	4	3	22	5	11.3	2.29
119	4348	1	1	1	1	150	90	60	2	5	4	24	2	11.3	2.29
120	1438958	1	1	1	1	140	80	67	2	4	3	22	5	7.8	2.93
121	1318401	1	1	2	1	160	80	78	2	4	3	22	6	7.9	5.83
122	1295112	1	1	2	2	160	80	73	2	4	3	20	1	8.1	2.92
123	1296110	1	1	2	2	160	80	68	2	4	3	20	1	7.6	2.92
124	1292650	1	2	2	2	110	70	64	2	5	5	26	0	10.5	3.68
125	128423	2	2	2	2	120	70	61	2	5	5	30	9	13.3	3.19
126	1301266	1	1	2	2	140	80	73	2	4	3	20	0	7.6	2.92
127	101294	2	2	2	2	120	70	75	2	5	5	30	4	13.3	3.19
128	985394	1	1	1	1	140	90	61	2	5	4	26	3	11.8	1.80

S_NO	ID	PLT	ALP	ALB	CA	C_CA	PTH	VITD	PHOS	UA	AMYLASE	LIPASE	U_CA	EF	FS
89	1049624	345	198	3.8	11.2	11.36	433	13	2.6	4.8	128	78	310	-	-
90	1256792	278	131	3.69	11.7	11.948	317.5	6.62	1.59	4.2	-	-	228	60	30
91	1261392	343	148	4.1	10.6	10.6	93.9	27.2	2.9	-	-	-	202	60	30
92	1248039	211	362	3.3	11.9	12.46	1624	11.7	2.6	7.8	-	-	198	60	30
93	1263047	283	120	4.66	11.2	11.2	701.3	26	3.3	7.5	-	-	219	60	30
94	1234540	168	152	4.51	11.9	11.9	323.7	13.61	2.87	6	-	-	245	60	30
95	1277431	232	167	4.6	10.8	10.8	156	5.5	3.5	5.6	134	231	267	-	-
96	802200	50	95	4.55	12.6	12.6	176.3	13	3.2	4.5	-	-	225	35	18
97	1259498	218	287	4.15	13.5	13.5	69.88	103	2.69	7.9	-	-	234	55	22
98	1285591	382	482	3.8	13.5	13.66	129.7	33	2.87	4.1	-	-	245	-	-
99	1289134	150	95	4.55	12.88	12.88	588	4.5	2.8	4.6	-	-	212	60	30
100	258175	200	144	3.2	9.9	10.54	1009	5.98	3.09	6.7	-	-	167	-	-
101	1291232	120	84	4.2	11	11	241	13	2.6	5.9	-	-	211	60	30
102	292149	158	129	4.2	10.03	10.03	1100	41.93	2.4	5.2	-	-	189	-	-
103	1294565	167	123	4.2	12	12	129.9	20	3.2	5.6	-	-	244	-	-
104	1291518	142	163	4.04	14.8	14.8	261.1	10.23	2.96	-	38	19	342	35	18
105	1237023	167	920	4.21	12.6	12.6	1503	23.53	1.4	-	-	-	212	45	24
106	1359922	177	139	4.46	15.5	15.5	2168	8.68	1.8	7.8	56	76	356	22	12
107	1367349	142	163	4.04	13.6	13.6	710	12	2.3	-	-	-	272.6	-	-
108	1382458	200	144	3.2	12.8	13.44	238	15	2.2	6.5	-	-	212	58	30
109	1381711	158	427	4.47	14.7	14.7	1207	26.85	1.3	7.8	-	-	353	60	30
110	1392365	206	110	4.68	13	13	567	12	1.6	7.9	-	-	296	48	23
111	1393730	66	105	3.92	11.7	11.764	206.7	13.89	2.4	6.7	1822	1140	212	60	30
112	1357365	142	163	4.04	14	14	842	16	2.3	-	-	-	359	-	-
113	1397513	150	357	2.18	14	15.456	2601	12.75	1.6	-	1886	2068	332	44	22
114	1405762	232	333	3.5	13.39	13.79	291	-	2.7	-	-	-	279	-	-
115	1413176	276	167	3.2	10.8	11.44	98.6	12	2.4	5.3	-	-	182	-	-
116	1413980	227	187	3.6	11.5	11.82	234	23	1.8	7.6	-	-	210	46	23
117	1426965	276	167	3.2	15.2	15.84	660.9	34	2.3	5.6	-	-	358	60	30
118	1428834	194	54	3.84	11	11.128	607.6	92	1.6	-	-	-	242	60	30
119	4348	260	144	4.18	11.6	11.6	641.3	12	2.2	6.4	134	245	212	46	23
120	1438958	454	124	3.4	11.2	11.68	140	23	2.6	6.7	-	-	189	36	23
121	1318401	346	139	4.46	12	12	813	13	2.3	6.7	-	-	212	46	23
122	1295112	120	84	4.2	11.5	11.5	163.3	26	1.7	7.2	-	-	189	-	-
123	1296110	80	84	4.2	13	13	576	26	1.5	7.2	-	-	256	46	23
124	1292650	120	158	3.2	11.3	11.94	137.2	16.8	2.2	6.7	34	45	193	46	23
125	128423	237	179	3.2	11.3	11.94	330.6	21.58	2.7	7.5	-	-	212	-	-
126	1301266	80	84	4.2	11.7	11.7	94	26	2.5	6.7	-	-	178	60	30
127	101294	342	119	4.95	11	11	71.18	38.5	2.2	6.7	-	-	187	-	-
128	985394	278	146	3	12.4	13.2	258.3	38.9	1.1	5.6	626	877	242	60	30

S_NO	ID	E	A	E:A	E_IVST(D)	E_LVID(D)	E_LVPW(D)	LVMI	PASP	AVC	X_RAY	USG_NECK	TC99
89	1049624	-	-	-	-	-	-	-	-	-	-	1	RIPA
90	1256792	35	44	0.80	1.4	4.6	1.4	149.87	12	2	2	1	RIPA
91	1261392	88	97	0.91	1.2	3.2	0.9	56.45	17	2	2	1	RSPA
92	1248039	80	60	1.33	0.9	4.9	1	96.81	56	1	2	1	RIPA
93	1263047	97	110	0.88	0.9	5.1	1	103.62	27	2	1	1	RIPA
94	1234540	69	90	0.77	1.2	4.5	1.2	115.85	32	2	2	1	RIPA
95	1277431	-	-	-	-	-	-	-	-	-	2	1	ECTOPIC
96	802200	94	110	0.85	0.8	4.9	1	90.24	25	2	2	-	LIPA
97	1259498	80	98	0.82	0.8	2.7	1	34.72	22	2	2	1	RIPA
98	1285591	-	-	-	-	-	-	-	-	-	2	1	LIPA
99	1289134	80	94	0.85	1	4.1	0.8	66.90	24	2	-	1	LIPA
100	258175	-	-	-	-	-	-	-	-	-	2	1	RIPA
101	1291232	35	44	0.80	1.4	4.6	1.4	149.87	31	2	2	1	RIPA
102	292149	-	-	-	-	-	-	-	-	-	-	1	RIPA
103	1294565	-	-	-	-	-	-	-	-	-	-	1	RIPA
104	1291518	94	125	0.752	0.8	4.9	1	90.24	25	2	2	2	LIPA
105	1237023	87	112	0.776785714	1.2	4	1	85.02	48	1	2	1	LIPA
106	1359922	88	112	0.785714286	1.2	4.4	1	98.87	65	1	2	1	RIPA
107	1367349	-	-	-	-	-	-	-	-	-	1	1	LIPA
108	1382458	89	101	0.881188119	1	4	0.9	69.18	16	2	2	2	LIPA
109	1381711	103	82	1.256097561	1.2	4.6	1.3	127.12	25	1	1	1	RIPA
110	1392365	68	75	0.906666667	0.9	4.5	0.9	78.12	21	2	1	1	LSPA
111	1393730	56	76	0.736842105	1.2	3.9	0.8	71.34	14	2	1	1	RIPA
112	1357365	-	-	-	-	-	-	-	-	-	1	1	LIPA
113	1397513	117	180	0.65	0.9	4.9	0.9	90.24	24	1	2	1	LIPA
114	1405762	-	-	-	-	-	-	-	-	-	-	2	ECTOPIC
115	1413176	-	-	-	-	-	-	-	-	-	1	1	LIPA
116	1413980	49	59	0.830508475	0.9	4.4	1	80.86	44	2	2	2	LIPA
117	1426965	58	98	0.591836735	1.1	3.9	0.7	61.63	34	2	1	1	RIPA
118	1428834	56	66	0.848484848	1.4	4.6	1.4	149.87	25	2	1	1	RIPA
119	4348	49	59	0.830508475	0.9	4.4	1	80.86	33	2	2	1	RSPA
120	1438958	49	87	0.563218391	0.7	4.1	0.8	52.59	11	2	-	1	LIPA
121	1318401	49	59	0.830508475	0.9	3.6	1	58.44	19	2	-	1	LIPA
122	1295112	-	-	#VALUE!	0	0	0	0.00	25	2	2	1	RIPA
123	1296110	49	59	0.830508475	0.8	4.4	1	75.23	14	2	2	1	RIPA
124	1292650	49	52	0.942307692	0.6	4.1	1	57.19	24	2	2	1	RIPA
125	128423	-	-	-	-	-	-	-	-	-	2	2	ECTOPIC
126	1301266	46	57	0.807017544	0.8	3.8	1.1	63.69	21	2	2	1	LIPA
127	101294	-	-	-	-	-	-	-	-	-	2	1	RIPA
128	985394	100	137	0.729927007	0.9	3.5	0.9	51.77	32	2	1	1	2

S_NO	ID	USG_WA	PT_MODE	IVF	FUROSE	CALCITO	CINACAL	ZOLEDRO	DENOSU	HD	CA_NOR_H	CA_NOR_Z	CA_NOR_D
89	1049624	CP	1	-	-	-	-	-	-	-	-	-	-
90	1256792	-	2	1	1	1	1	1	2	2	7	2	-
91	1261392	NS	2	1	1	2	1	2	2	2	8	-	-
92	1248039	RC	2	1	1	1	1	1	2	2	16	6	-
93	1263047	RPC	2	1	2	2	1	2	2	2	12	-	-
94	1234540	-	2	1	1	1	1	2	2	2	13	-	-
95	1277431	CP	2	2	2	2	2	2	2	2	-	-	-
96	802200	RPC	2	2	1	1	2	2	2	2	7	-	-
97	1259498	RPC	2	1	1	1	1	1	2	2	12	4	-
98	1285591	NS	2	1	1	1	1	2	2	2	6	-	-
99	1289134	NS	1	-	-	-	-	-	-	-	-	-	-
100	258175	RC	2	1	1	1	1	2	1	2	12	-	5
101	1291232	NS	2	1	1	1	1	1	2	2	8	3	-
102	292149	NS	1	-	-	-	-	-	-	-	-	-	-
103	1294565	-	1	-	-	-	-	-	-	-	-	-	-
104	1291518	NS	2	1	2	2	1	2	2	2	7	-	-
105	1237023	RPC	2	1	1	1	1	2	1	2	7	-	3
106	1359922	NS	2	1	1	1	1	2	1	2	9	-	4
107	1367349	NS	2	1	1	1	2	1	2	2	13	4	-
108	1382458	RC	2	1	1	1	1	2	2	2	8	-	-
109	1381711	-	2	1	1	1	1	2	2	2	9	-	-
110	1392365	-	2	2	1	1	1	1	2	2	13	4	-
111	1393730	RC	2	1	1	1	2	2	2	2	10	-	-
112	1357365	NS	1	-	-	-	-	-	-	-	-	-	-
113	1397513	AP	2	1	1	1	1	2	1	1	23	-	6
114	1405762	-	1	-	-	-	-	-	-	-	-	-	-
115	1413176	NS	1	-	-	-	-	-	-	-	-	-	-
116	1413980	-	2	1	1	2	2	2	2	2	12	-	-
117	1426965	NS	2	1	1	1	1	1	2	2	12	5	-
118	1428834	-	2	1	1	1	1	2	1	2	8	-	4
119	4348	CP	2	1	1	1	1	2	2	2	6	-	-
120	1438958	RC	1	-	-	-	-	-	-	-	-	-	-
121	1318401	NS	1	-	-	-	-	-	-	-	-	-	-
122	1295112	RC	2	2	2	1	1	2	1	2	9	-	3
123	1296110	NS	2	2	2	1	1	1	2	2	9	3	-
124	1292650	RC	2	1	1	1	1	1	2	2	14	4	-
125	128423	RC	2	1	1	1	1	2	2	2	10	-	-
126	1301266	NS	2	2	2	1	1	1	2	2	9	3	-
127	101294	RC	2	1	1	1	1	2	2	2	8	-	-
128	985394	AP	2	1	1	1	1	1	2	2	12	5	-

S_NO	ID	SURGERY	HBS	HBSCA	HIS_SZ_A	HIS_SZ_B	HIS_SZ_C	HIS_WT	HIS_S/O	OUTCOME	FU_CA	FU_CCA	FU_PTH
89	1049624	2	-	-	-	-	-	-	-	FU	10.9	11.14	4.8
90	1256792	1	2	-	2	1	1	0.4	PA	FU	9.7	9.94	15.03
91	1261392	1	2	-	3.5	1.4	0.1	6	PA	FU	9.7	9.94	3.5
92	1248039	1	2	-	3	3	0.5	10	PCA	FU	11	11.24	213
93	1263047	1	2	-	1.2	0.8	0.5	2	INC	FU	9.5	9.74	14
94	1234540	1	2	-	1.5	0.6	0.2	3	PA	FU	8.2	8.44	3.9
95	1277431	1	2	-	1.2	0.3	0.1	2	PA	FU	8.9	9.14	3.2
96	802200	1	2	-	1	0.5	0.3	2	PA	FU	8.5	8.74	14.86
97	1259498	1	2	-	1.8	1	0.6	4	PA	FU	8.7	8.94	12
98	1285591	1	2	-	0.8	0.6	0.3	2	PA	FU	9.5	9.74	4.7
99	1289134	2	-	-	-	-	-	-	-	FU	8.6	8.84	12
100	258175	1	2	-	3.6	2.8	0.9	12	PA	FU	8.4	8.64	3.2
101	1291232	2	-	-	-	-	-	-	-	FU	8.8	9.04	19.2
102	292149	2	-	-	-	-	-	-	-	LTFU	-	-	-
103	1294565	2	-	-	-	-	-	-	-	FU	8.7	8.94	12
104	1291518	1	2	-	4	3	2	18	PA	FU	8.9	9.14	7.18
105	1237023	1	2	-	4.5	3	2.5	12	PA	FU	8.7	8.94	13.4
106	1359922	1	2	-	4	3.5	2	4.6	PA	FU	8.3	8.54	10.2
107	1367349	2	-	-	-	-	-	-	-	FU	10.7	10.94	45
108	1382458	1	2	-	2.4	1	0.8	4.9	PA	FU	9.6	9.84	23
109	1381711	1	2	-	4	3	1	0.2	PA	FU	8.8	9.04	6
110	1392365	1	2	-	7	2	1.5	12	PA	FU	8.2	8.44	1
111	1393730	1	2	-	1.2	0.7	0.2	1.6	PA	FU	8.8	9.04	12
112	1357365	2	-	-	-	-	-	-	-	FU	8.9	9.14	19
113	1397513	1	1	5.6	3.5	2.8	1	4.8	PA	FU	7.5	7.74	9.5
114	1405762	2	-	-	-	-	-	-	-	LTFU	-	-	-
115	1413176	2	-	-	-	-	-	-	-	FU	8	8.24	4.6
116	1413980	1	2	-	3.4	2.8	1.3	13	PA	FU	12	12.24	898
117	1426965	1	2	-	1.2	0.8	0.4	13	PA	FU	8.4	8.64	5.6
118	1428834	1	2	-	2.1	1.5	0.4	6	PA	FU	8.8	9.04	21
119	4348	1	2	-	3.6	2.5	1.2	5	PA	FU	8.4	8.64	7.6
120	1438958	2	-	-	-	-	-	-	-	FU	10.8	11.04	69
121	1318401	2	-	-	-	-	-	-	-	FU	11	11.24	89
122	1295112	2	-	-	-	-	-	-	-	FU	8.7	8.94	2.97
123	1296110	2	-	-	-	-	-	-	-	FU	9.1	9.34	18.9
124	1292650	2	-	-	-	-	-	-	-	FU	8.8	9.04	12
125	128423	1	2	-	1.3	0.9	0.2	5	PA	FU	8.4	8.64	11
126	1301266	2	-	-	-	-	-	-	-	FU	9.1	9.34	17.3
127	101294	1	2	-	2.1	1.7	0.7	5	PA	FU	8.8	9.04	12
128	985394	1	2	-	0.8	0.5	0.4	6	INC	FU	8.5	8.74	12

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Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Harmanjot Kaur Walia**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To study the clinical profile of patients presenting with primary hyperparathyroidism .

Supervisor
Dr. Vipin Kumar
Assoc. Prof.,
Dept. of Medicine

Co-Supervisor:-
Dr. Sandeep Puri
Professor
Dept. of Medicine

Co-Supervisor:-
Dr. Saurabh Arora
Asst. Professor
Dept. of Endocrinology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

GENERAL MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022

DR. HARMANJOT KAUR WALIA

DEPARTMENT OF GENERAL MEDICINE
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM
For the degree of	MD GENERAL MEDICINE
Name of the candidate	Dr. Harmanjot Kaur Walia
Supervisor	Dr. Vipin Kumar, Associate Professor, Department of Medicine, DMCH, Ludhiana
Co-Supervisor	Dr Sandeep Puri, Professor, Department of Medicine, DMCH, Ludhiana Dr Saurabh Arora, Assistant Professor, Department of Endocrinology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Primary hyperparathyroidism refers to inappropriate or unregulated overproduction of parathormone resulting in increased renal absorption of calcium, leading to phosphaturia, increased synthesis of 1,25 dihydroxy vitamin D (which increases intestinal calcium absorption) and increased bony resorption ultimately resulting in hypercalcemia.

Aims and Objectives: The proposed research aims to evaluate clinical profile of patients presenting with primary hyperparathyroidism in tertiary care hospital in North India.

Materials and Methods: This prospective cross sectional observational study will be conducted at DMCH Ludhiana between 15th September 2022 to 31st Dec 2023. Study group will include patients admitted in hospital or presenting to OPD, Such patients will be assessed for their clinical presentation and outcome in accordance with treatment provided.

Clinical significance: Primary Hyperparathyroidism is third most common endocrine disorder after diabetes and thyroid disorders constituting 0.1 % prevalence yet it is one of the most common conditions to be underdiagnosed and undertreated

Keywords: Primary Hyperparathyroidism, North India, Pancreatitis, Osteitis fibrosa cystica, nephrolithiasis, depression anxiety, cinacalcet, denosumab

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM"** exist in the Department of General Medicine at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

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APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
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Department	General Medicine
Topic of Thesis	TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM
Likely date of appearing in PG examination	MAY, 2024
Date of enrollment	MARCH 7, 2022
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Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
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Approved: Yes / ~~No~~

Dr. Sandeep Puri
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Approved: Yes / ~~No~~

Prof. Arvind Malhotra
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BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT
PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. HARMANJOT KAUR WALIA HOUSE NO.1147/2 , KRISHNA NAGAR, CIVIL LINES , LUDHIANA
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL
3	COURSE OF STUDY AND SUBJECT	M.D. GENERAL MEDICINE
4	DATE OF ADMISSION OF COURSE	01/02/2022
5	TITLE OF THE TOPIC	TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Primary Hyperparathyroidism is third most common endocrine disorder after diabetes and thyroid disorders constituting 0.1 % prevalence yet it is one of the most common conditions to be underdiagnosed and undertreated.[1]

Alex Dombrowsky et al.[2] made very important contribution to the literature on hyperparathyroidism, they outlined the key reasons for underdiagnosis and undertreatment among older patients. It was ultimately found that hypercalcemia on routine laboratory evaluation (the most common presentation of hyperparathyroidism) is frequently overlooked, inadequately evaluated, and often attributed to causes other than hyperparathyroidism. Primary finding was that very few patients with hypercalcemia undergo evaluation of PTH levels to identify the underlying etiology, and an even smaller minority with both abnormal calcium and PTH are referred to surgeons to discuss treatment. So basically understanding the barriers to diagnosis and surgical referral is a necessary step toward designing interventions to ensure that patients are treated in a timely fashion that optimizes quality of life by minimizing exposure to disease-related morbidity.

Untreated hyperparathyroidism increases the risk of fractures and kidney stones, is associated with depression and cognitive impairment, and can cause cardiovascular dysfunction that leads to hypertension, stroke, and myocardial infarction which can greatly impair quality of life. Furthermore the occurrence of acute parathyroid crisis in literature has been explained with risk of 52.5% mortality.[3]

The diagnosis of hyperparathyroidism requires the ability to interpret the relationship between calcium and parathyroid hormone (PTH) levels, and this can be a complex calculation that requires expert assistance as in presence of hypercalcemia even PTH in normal range above 20 contributes to nonclassical hyperparathyroidism as with hypercalcemia PTH levels are bound to be subnormal i.e <20 hence

inappropriately normal level of PTH account for most commonly ignored population delaying diagnosis. In addition another reason for undertreatment includes non-surgeon's overestimation of the risks of surgery or underestimation of the benefits to patients.

There are striking discrepancies around the world with respect to incidence, symptoms, and complications of PHPT. In developing countries, particularly India, PHPT is still an uncommonly diagnosed, overtly symptomatic disease of "bones, stones, abdominal groans, and psychic overtones." This may be due to the fact that, in India, screening of the healthy population for hypercalcemia is not a routine practice and there is limited access to medical treatment especially in the rural areas. Pradeep, et al[4] in Systematic Review of Primary Hyperparathyroidism in India (2011) stated that Primary hyperparathyroidism (PHPT) has become an asymptomatic disease in the Western world with the introduction of routine calcium screening. However, the same phenomenon is not observed in India. They systematically reviewed the status of PHPT in India. While there is a paucity of literature on PHPT from India as compared to Western countries, most patients present with symptomatic disease whereas very few are screen-detected cases (bone disease 77%, renal disease 36%, and 5.6% asymptomatic). Worldwide, the presentation of PHPT has changed from a symptomatic to an asymptomatic disease. As a result, newer guidelines are being laid down to decide on indications for surgery in asymptomatic disease. In India, however, asymptomatic presentation is virtually unheard of. Even the symptomatic disease is picked up late after a series of management for fractures and renal stones by the orthopedic surgeons and the urologist.

Moreover limited studies have been conducted on primary hyperparathyroidism in entire world with even lesser proportional studies conducted in India in very few centers.Limited research has been conducted and published in India when compared to UK, USA, and AUSTRALIA. Majority of research includes case reports or case series; with limited articles available on overall complete clinical profile. Being a disease with serious complications and major morbidity. Indian

physician needs to develop a high index of suspicion . So, we need to develop our own guidelines to diagnose PHT effectively in the face of economic, social, educational, awareness and availability issues. [5]

So this study is basically designed to accomplish need to assess changing profiles of clinical manifestations i.e. to analyse relative asymptomatic shift in Indian population(review of Indian subcontinent states only 5.6% asymptomatic detections). Moreover this study aims to act as a source of reference in this underpublished and knowledge deficient arena.

6.2 REVIEW OF LITERATURE

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder, after diabetes and thyroid diseases and affects up to 0.1% of the general population. [1] Primary hyperparathyroidism refers to inappropriate or unregulated overproduction of parathormone resulting in increased renal absorption of calcium, leading to phosphaturia, increased synthesis of 1,25 dihydroxy vitamin D (which increases intestinal calcium absorption) and increased bony resorption ultimately resulting in hypercalcemia. Historically with the advent of multichannel biochemical screening in the 1970s, the incidence of PHPT increased around the world. Subsequently the clinical entity of asymptomatic hyperparathyroidism was recognized.[2] There are striking discrepancies around the world with respect to incidence, symptoms, and complications of PHPT.

In developing countries, particularly India, PHPT is still an uncommonly diagnosed, overtly symptomatic disease of “bones, stones, abdominal groans, and psychic overtones.” This may be due to the fact that, in India, screening of the healthy population for hypercalcemia is not a routine practice and there is limited access to medical treatment especially in the rural areas. Series of patients with PHPT from developed nations are largely dominated by elderly females with mild to moderate hypercalcemia and very few with classical symptoms [4] which is contrary to the clinical picture seen in developing countries, especially India. Demographically on analysis of Indian series, females were commonly affected (1.7 : 1, F : M).Limited research has been conducted and published in India as compared to UK, USA, and AUSTRALIA. Majority of research includes case reports or case series; with limited articles available on overall complete clinical profile. Unique presentations have been discussed and that information will be used as basic building block in our study.[6]

CLINICAL PROFILE-

ABDOMINAL GROANS-Saurabh Arora et al[7] published case series of 30 patients with acute pancreatitis as initial manifestation of primary hyperparathyroidism where need of timely diagnosis to prevent repeat

attack was highlighted. It was *concluded* that patients with PHPT associated pancreatitis had male preponderance, higher calcium levels and lower frequency of skeletal involvement as compared to PHPT patients without pancreatitis. Presence of nephrolithiasis was significantly associated with severe pancreatitis. One patient had refractory hypercalcemia associated with renal failure and was successfully managed with denosumab. PHPT masquerading as acute pancreatitis is rare and high index of suspicion is required to diagnose this condition especially in the presence of normocalcemia at presentation. Incidence of pancreatitis ranges from 1.5-12 % of the patients.

On review of literature various studies have stated high prevalence of constipation in patients with primary hyperparathyroidism. Positive association also seen with peptic ulcer disease in approximately 9% patients and resolution of symptoms post parathyroidectomy has been established.

STONES-Raiz Ahmad Misgar et. al[8] aimed to characterize patients with PHPT with nephrolithiais and to compare patients with silent and symptomatic stones.They reviewed clinical data of 186 patients with PHPT. Silent renal stones were defined as ultrasonography finding of renal stones without symptoms. Symptomatic renal stones were defined as those with symptoms or a history of graveluria or any procedure for nephrolithiasis. A 5-mm diameter was set as the cut-off between micro- and macrolithiasis. It was concluded that patients with silent renal stones had significantly lower serum calcium and higher phosphate, than those with symptomatic stones. Most (75%) patients with silent renal stones had microlithiais, while only a fifth (22%) with symptomatic renal stones had microlithiasis. Most patients with silent renal stones had microlithiasis and biochemical features of less severe disease. Patients with silent renal stones may represent early mild stage of PHPT.Incidence of nephrocalcinosis and nephrolithiasis is 7%, progression of stones is mostly reversed in majority of cases after parathyroidectomy. Renal insufficiency measured as decreased eGFR <60 ml/minis relatively common (17%). Simple renal cysts are benign

complications and are hypothesised to be due to chronic PTH action on tubular epithelium.

BONES- Yu Wang et al[9] reported rare case report of severe bone disease caused by primary hyperparathyroidism where a 33-year-old male presented with pain and restricted mobility in his right upper limb and right hip due to a trivial fall. Computed tomography examination showed a supracondylar fracture of the right humerus, a fracture of the right femoral neck and multiple brown tumors. Ultrasonography of neck showed a 3.5- × 1.6-cm hypoechoic mass below the left lobe of the thyroid. The patient was diagnosed with primary hyperparathyroidism based on increased serum calcium and parathormone concentrations, pathological fractures, and multiple brown tumors. He therefore underwent bilateral lower parathyroidectomy. Pathological examination revealed a parathyroid adenoma. The patient recovered well after surgery and was followed up for 6 months with no symptoms of hyperparathyroidism. From this it can be concluded that clinicians should be aware of the possibility of severe bone disease secondary to primary hyperparathyroidism. Active and early diagnosis and surgical treatment are important in such cases.

Bone disease is classically called as osteitis fibrosa cystica with signs and symptoms including bony pains, pathological fractures, proximal muscle weakness with hyperreflexia. Patient may present with salt pepper skull, bony erosion and resorption of phalanges.

PSYCHIC OVERTONES-Neuropsychiatric assessment is present hotspot of research especially in India. A. Goyal et al[10] stated wide variety of psychiatric symptoms ranging from mild personality changes to severe depression and psychosis in patients of PHPT. However, the psychiatric profile in Indian patients remains a mystery. Study was aimed to see if surgery can alleviate the psychiatric morbidity and improve the quality of life of patients. It was concluded that the psychologic symptom distress is multidimensional and symptoms significantly improved by 6 weeks post parathyroidectomy. There was no memory and intelligence impairment in any of the groups pre or post

operatively. No correlation was found between serum calcium levels and psychiatric morbidity.

Recent studies include Jessica et al[11] Study was conducted in view of poorly defined outcome of parathyroidectomy on neuropsychiatric symptoms in primary hyperparathyroidism . The validated scales Patient Health Questionnaire-9 and Generalized Anxiety Disorder-7 were used to assess depression and anxiety, respectively. It was concluded that patients undergoing parathyroidectomy showed significant improvement in neuropsychiatric symptoms after surgery. Neuropsychiatric symptoms are more prevalent in patients with primary hyperparathyroidism. Neuropsychiatric symptoms should be assessed in all patients with primary hyperparathyroidism and should be considered a relative indication for parathyroidectomy.

RARE PRESENTATIONS-

Yun Xu et al[12] presented case report of 31 year old second trimester pregnant patient presenting with brown tumour of left lower leg with hypercalcemic crisis attributable to primary hyperparathyroidism due to parathyroid adenoma. The patient was supported on continuous renal replacement to reduce ionized calcium level. Parathyroidectomy was performed at the 19th week of gestation. Threatened abortion occurred 2 days after the surgery, and magnesium sulphate was used to prevent the abortion. Calcium gluconate, calcium carbonate and vitamin D3 were used to treat the hypocalcemia that occurred 5 days after the surgery.It was concluded that maternal PHPT is rare and challenging to diagnose and can cause life-threatening complications to mother and fetus and decision regarding surgery for a pregnant woman with primary hyperparathyroidism is more complex than in men or nonpregnant women.

DK Kar et al[13] reported unusual patient of parathyroid carcinoma with cerebral and pulmonary metastasis with metastasis contributing to 16% mortality in post parathyroidectomy in phpt patients.

Data from SGPGIMS[14], India revealed fractures in 57% of the patients, brown tumors in 49%, and 27% of patients were crippled (due to multiple fractures). Combined bone and kidney disease was seen in

36% of patients, psychiatric symptoms in 38%, and palpable neck masses in 33%. Bhansali et al. [15] have observed similar figures from another premier institute in India where 67% had bone disease, 48% had fractures, 21% had stone disease, 23% had psychiatric symptoms and 15% had peptic ulcer.

LOCALISATION STUDIES-

There is a paucity of literature on localization studies in all the Indian publications still the reported data are in accordance with the published literature from Western series. Neck ultrasound has been reported to localize the adenoma in 65–77% of patients.[16,17] Methyl isobutyl isonitrile (MIBI) scan positivity has been reported in 86.9– 100%.[17] Thallium-201 Technetium-99 pertechnetate subtraction has been reported to have a sensitivity of 87–100% . Contrast-enhanced computerized tomography (CECT) of the neck has a sensitivity ranging from 65% to 93.5% in localizing parathyroid adenoma. The reported sensitivity of ultrasound of the neck has been low in India, which could be due to the absence of a dedicated parathyroid sonologist. Therefore, the numbers of cases diagnosed/operated on are far less than what is reported from the developed nations. MIBI and USG neck are more commonly being done now.

SURGICAL APPROACH (PARATHYROIDECTOMY)-

The approach has ranges from bilateral conventional neck exploration involving four gland exploration to minimally invasive exploration to endoscopic focused parathyroidectomy. Recurrent PHPT has ranged from zero to 4.16% and persistent PHPT between zero and 2.7%.[14,15,18]

PATHOLOGY OF SPECIMEN-

On review of literature pathological specimen weight has been reported differently especially in Indian and western studies. Developed countries show the average tumor weight was 2–4 gm. Among Indian patients, the tumor weight ranged from 1.25 to 102 gm.[19] The prevalence of adenoma, hyperplasia, and carcinoma is 89.1%, 6.56%, and 4.37%, respectively.[20] The incidence of parathyroid carcinoma

causing PHPT in the various series has been 2.6 to 6%. This is higher than that observed from developed countries (1%).[21]

POSTOP-

Postoperative hungry bone syndrome (HBS) has been observed in 24% to 82% of the cases. The immediate postoperative period is turbulent in Indian PHPT patients due to HBS, postoperative pancreatitis, sepsis, multiorgan failure, metabolic disturbances related to the end-stage renal disease, and thrombophlebitis related to intravenous calcium infusions. In contrast to this, parathyroidectomy in the Western series is an outpatient procedure with the majority getting discharged the same day.[14-16,20] Anemia and marrow fibrosis improved after curative parathyroidectomy in a series of 28 patients at three months follow up.[22]

So, we can conclude as of now, majority of patients diagnosed with PHPT in India have symptomatic disease. The mean calcium, PTH, and alkaline phosphate levels are higher with low Vit D levels with Vit D deficiency contributing to the severity of bone disease. HBS in the postoperative period necessitates intravenous calcium supplements and prolonging hospital stay, resulting in higher morbidity. Patients can benefit from early diagnosis of mild and asymptomatic PHPT only if more efforts are taken to identify these cases. For this, efforts are needed to incorporate calcium screening in the routine health check-ups. The increasing parathyroid awareness among physicians as evidenced by the increase in the number of publications on PHPT will help in diagnosing more cases.

6.3 AIMS AND OBJECTIVES OF THE STUDY

- The proposed research aims to evaluate clinical profile of patients presenting with primary hyperparathyroidism in tertiary care hospital.

7. MATERIALS AND METHODS

7.1 Source of Data:

This prospective cross sectional observational study will be conducted at DMCH Ludhiana between 15th September 2022 and 31st December 2023. Study group will include patients admitted in hospital or presenting to OPD.

7.2 METHOD OF COLLECTION OF DATA

Inclusion Criteria –

All patients with atleast one Corrected Serum Calcium level of >10.2 mg/dl with PTH levels >20 ng /dl.

Exclusion criteria excludes patients with-

1. Serum Creatinine >2.5 with evidence of chronic kidney disease (rule out secondary primary hyperparathyroidism)
2. Kidney transplant patients or recipients of cyclosporine, tacrolimus, sirolimus (rule out tertiary hyperparathyroidism)
3. History of invasive carcinoma.

Methodology

Such patients will be exposed to various data collection methods:

In addition to obtaining detailed medical history regarding symptoms and duration, examination of patient especially CNS power assessment along with MMSE will be done. Any significant past history in the form of HTN, Diabetes, Coronary artery disease, Cerebrovascular accident will be recorded for all the subjects. Blood samples obtained by venepuncture will be subjected to routine investigations (CBC, RFT, LFT) with special interest to serum calcium, serum PTH, Serum Vitamin-D, Serum Uric Acid levels. Urine examination will be done with special interest to 24 hour urinary calcium. X Ray (B/L hand and wrist) will be done along with USG neck .Patient further will be subjected to Tc 99 SESTAMIBI SPECT scan to localise the lesion.

For outcome analysis medical treatment option selected for each patient will be analysed with regards to time taken for normalisation of

calcium levels. In case of surgical management time to surgery, type of surgery, pathological features of resected specimen and incidence of post op hungry bone syndrome will be documented for comparison with international and national standards.

OUTCOME

This study aims to evaluate clinical profile to create awareness to increase index of suspicion to make early diagnosis, moreover outcome with different management strategies will also assessed according to time taken to normalise calcium post drug administration. It would help in formulating new and concise diagnostic and therapeutic protocols helping in early diagnosis and decreasing patient morbidity

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ± standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Blood samples obtained by venepuncture will be subjected to routine investigations (CBC, RFT, LFT) with special interest to serum calcium, serum PTH, Serum Vitamin-D, Serum Uric Acid levels. Urine examination will be done with special interest to 24 hour urinary calcium. X Ray (B/L hand and wrist)will be done along with USG neck .Patient further will be subjected to Tc 99 SESTAMIBI SPECT scan to localise the lesion

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Sr. No.

Name: Age: Sex:

MRD No.:

Phone no.:

Occupation:

Address:

History:

	Symptoms		
1	Stones	Hematuria Polyuria H/o Renal stones	
2	Bones	Bony pains H/o fracture	
3	Abdominal Groans	Pain abdomen Constipation	
4	Psychic Overtones	Depression Anxiety	
5	Asymptomatic	No symptom present	

Past History:

1	Diabetes mellitus (DM)	
2	Hypertension (HTN)	
3	Coronary artery disease (CAD)	
4	Cerebrovascular accident (CVA)	

Signature of candidate **Signature of supervisor**

Examination:

GPE:			
Systolic BP: Diastolic BP:		Heart rate:	
Local Examination:			
Neck mass:			
Jaw swelling:			

CNS:	
Proximal muscle power:	
Distal muscle power:	
Deep tendon reflexes:	
MMSE:	
PHQ4	

Investigations:

S.No.		Normal range	Patient value	Analysis
1. CBC:				
1 A.	Haemoglobin			
1 B.	TLC Neutrophil LymphocyteNLR			
1 C.	Platelet count			
2.RFT:				
2 A.	Urea			
2 B.	Creatinine			
2 C.	Serum sodium			

Signature of candidate **Signature of supervisor**

2 D.	Serum potassium			
3.LFT:				
3 A.	Bilirubin (total)			
3 B.	SGOT			
3 C.	SGPT			
3 D.	ALP			
3 E.	Albumin			
4.	Serum calcium			
5.	Serum PTH			
6.	Serum Vit-D			
7.	Phosphorous			
8.	S. Uric acid			
9.	S. Amylase			

10.	S.Lipase			
11. URINE ROUTINE EXAMINATION				
11A.	pH			
11B.	RBC			
11C.	WBC			
11D.	Proteins			
12.	24hr urinary ca			
13. X-Ray (both hand with wrist)Impression:				
14. USG Neck Impression:				
15. USG Whole AbdomenImpression:				
16. 2D Echo Impression:				

Signature of candidate **Signature of supervisor**

17. Tc 99 sestamibi spectImpression:

TREATMENT GIVEN FOR HYPERCALCEMIA:

IV fluids	
Calcitonin	
Furosemide	
Zolendronic acid	
Hemodialysis	
Denosumab	

TIME TO NORMALISATION OF CALCIUM:

After hospitalisation	
After zolendronic acid	
After denosumab	

FOLLOW UP (1MONTH-6 MONTH)

S.Calcium		S.PTH	

Signature of candidate **Signature of supervisor**

INFORMED PATIENT CONSENT

Date: _____

I…….D/o, W/o, S/o……..…… am willing to participate in the study **"TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____	_____
गवाह के हस्ताक्षर	रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:	नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“TO STUDY THE CLINICAL PROFILE OF PATIENTS PRESENTING WITH PRIMARY HYPERPARATHYROIDISM” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ